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A TECHNIQUE FOR SPLANCHNIC RESECTION FOR HYPERTENSION

PRELIMINARY REPORT

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A NUMBER of methods of interrupting the splanchnic nerves in the hope of relieving hypertension have been reported in the past five or six years. Four different approaches have been suggested: intraspinal anterior root section, supradiaphragmatic splanchnic resection, subdiaphragmatic splanchnic resection, and celiac ganglionectomy.[1-6]

Our experience with these operations in approximately 150 cases of hypertension, coupled with our experience in the treatment of peripheral vascular disease by sympathectomy in several hundred cases, leads us to feel that sympathectomy yields its best results when the operation is (a) adequately complete, (b) preganglionic in type, and (c) extensive enough to guard against future regeneration of interrupted pathways.

An operation for hypertension, in our opinion, should fulfill these qualifications as far as possible, and in addition should include careful exploration of the kidneys, the adrenal glands, and the paravertebral regions. It is desirable to obtain all possible information regarding renal pathology in this disease. It is also well to exclude adrenal tumors and paragangliomas from the picture. Moreover, an operation should subject a patient to the least risk possible and should have no serious untoward effects.

In judging the results of sympathectomy for peripheral vascular disease, many objective tests are available which enable one to determine the completeness of a given operation. In the case of hypertension it is different. Symptomatic relief, changes in eyegrounds, renal function, and cardiac function are not very accurate guides as to the completeness of the interruption of splanchnic nerves. The change which

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is produced in blood pressure levels would appear to be the only reliable method of judging the completeness of the operation.

It has been our impression that complete or nearly complete splanchnic resection in man should result in a characteristic change in blood pressure in every patient with hypertension. We know that the splanchnic bed is man's mechanism for maintaining his blood pressure level relatively constant in the lying, the sitting, and the standing positions. If the splanchnic bed is well denervated, the blood pressure level should fall as the patient changes from the lying to the sitting and standing positions. Such a change has followed splanchnic resection by laminectomy and anterior root section, although this operation, in addition to interrupting sympathetic motor pathways, also divides somatic motor pathways. The latter results in extensive muscular paralysis.

Unless a postural change in blood pressure follows splanchnic resection, one cannot be certain that the maximum change in blood pressure level in the various positions has been produced. If the splanchnic bed is thoroughly denervated in man, one can perhaps also feel reasonably certain that the kidneys and the adrenal glands have been denervated as well.

Because the various operations which we had employed did not consistently produce significant postural changes or produce comparable blood pressure changes in similar cases in the horizontal position, we have been varying these procedures during the past two years in order to determine the minimal operation which would always cause a postural change in blood pressure and still fulfill the other qualifications which we felt were important.

Cases which had had a supradiaphragmatic splanchnic resection without any effect upon the blood pressure level were subjected to further surgery. At the original operation, the communicating rami of the tenth, eleventh, and twelfth dorsal segments were divided, removing the sympathetic trunk from above D10 to below D12, and removing as liberal a portion of the great splanchnic nerve as could be obtained through an eleventh rib exposure. This procedure was done on both sides. At a second operation, the upper three lumbar ganglia were removed by a subdiaphragmatic extraperitoneal approach, on each side, in two stages. In some instances, this resulted in a definite lowering of the blood pressure level with a marked postural change. In other instances there was no significant effect on the blood pressure level. This led us to feel that there must be a significant motor supply to the splanchnic bed coming from above either operative areas. That this was so was ascertained by proceeding with further interruption of the mid- and upper thoracic sympathetic chains in several cases with total sympathectomy (removal of the sympathetic trunk from above C3 to below L3 on both sides) in one case. It was determined that, if the splanchnic bed was thoroughly denervated, a postural change in blood

pressure levels would result. These experiences led us to believe that there were many anatomical variations from patient to patient. The same portion of the splanchnic nerve supply was apparently not equally significant in each case. It seemed probable, however, that an operation could be done which would cover the various anatomical variations.

Our impression of the anatomical pathways to the splanchnic bed is shown in Fig. 1. It was found that adequate exposure of this entire region could be obtained by resecting the twelfth rib, through a hockey-stick incision. The upper portion is vertical, about two inches lateral to the midline, running up over the inner end of the eleventh rib. The

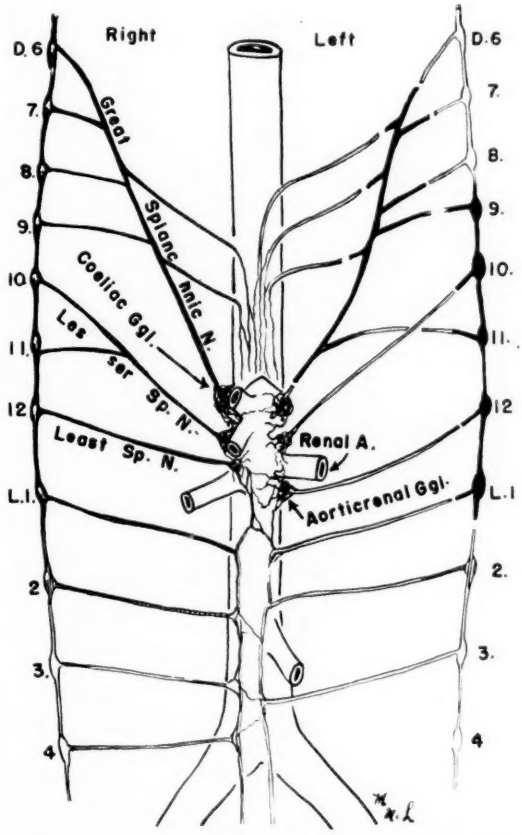

Fig. 1.—A diagrammatic sketch of the nerve supply to the splanchnic bed. On the left side the area to be removed on both sides is blacked out. This is the minimal procedure which we have found to be followed consistently by an immediate postural change in blood pressure.

lower portion curves laterally, one-half inch below and parallel to the twelfth rib. The sheath of the sacrospinalis muscle is opened vertically to below the twelfth rib, and dissection is then carried laterally following the skin incision through the deeper structures below and beyond the tip of the rib. The twelfth rib is removed from the transverse process to the lateral border of the sacrospinalis sheath. The twelfth intercostal artery, vein, and nerve are resected over a similar area. The diaphragm is divided from its lateral border to the spine,

one inch below and parallel to the pleural reflection. The pleura is then separated from the thoracic cage up to the middorsal region.

The kidney then is readily exposed and inspected. An excellent view is obtained of the entire organ including its pedicle. The adrenal gland is readily seen and explored. The sympathetic trunk and paravertebral region are exposed from D9 to below L2. The great splanchnic nerve can be seen from its insertion in the celiac plexus upwards for virtually its entire extent, with its important branches running to the aorta above the diaphragm. The exploration having been completed, the desired portion of the splanchnic supply is then removed, the diaphragm resutured, and the wound closed in layers with silk technique. Intratracheal anesthesia is used. The operation is done in two stages between one and two weeks apart. Since September, 1938, this operation has been used in a series of twenty-six cases. There has been no operative mortality. There have been no serious complications.

These cases may be divided into three groups. In all, virtually the entire great splanchnic nerve was removed from its insertion in the celiac ganglion upward to the midthoracic level. The ganglion was not disturbed, but care was taken to divide all branches running from the great splanchnic nerve to the aorta above the diaphragm. Different portions of the sympathetic trunk itself were removed in each group, in order to complete the denervation of the splanchnic bed and to ascertain the minimal procedure which would consistently produce the desired effect. In Group A cases (Table I) the communicating rami of D9, D10, D11, and D12 were sectioned, and the sympathetic trunk was removed over this area.

TABLE I*

GROUP A

NO. CASES	STAGE OF DISEASE	POSTURAL CHANGE IN BLOOD PRESSURE
1	Group I	Moderate
2	Group II	Slight
3	Group II	Insignificant
4	Group II	Insignificant
5	Group IV	Moderate
6	Group IV	Insignificant

**Operation*—Bilateral excision of virtually the entire great splanchnic nerve from its insertion in the celiac plexus upwards to the middorsal level with division of all aortic branches above the diaphragm. Interruption of the communicating rami of D9, D10, D11, D12, with excision of the sympathetic trunk over this area. In all tables the cases are divided into four groups according to the stage of the disease. This division is based largely upon eyeground changes. Group I cases have minimal evidence of change in the retinal arterioles, chiefly vasoconstriction, with no change in the heart or kidneys. Group II cases have more marked retinal change with caliber variation in the arterioles, nicking at the venous crossings in addition to vasoconstriction. There is no hemorrhage or exudate in cases in Groups I and II. In Group II there may be slight enlargement of the heart and minimal evidence of altered renal function. Group III cases show hemorrhage and exudate in the eyegrounds and enlarged hearts, usually with coronary changes; some have had a cerebral accident, and usually show some evidence of impaired renal function. Group IV cases are those in the malignant phase of the disease, who, in addition to those changes which are usually present in Group III, also show edema and elevation of the disk.

In Group B cases (Table II) the communicating rami of D9, D10, D11, D12, and L1 were divided, removing the sympathetic trunk over this area.

TABLE II

GROUP B

NO. CASES	STAGE OF DISEASE	POSTURAL CHANGE IN BLOOD PRESSURE
1	Group II	Moderate
2	Group II	Marked
3	Group II	Moderate
4	Group II	Moderate
5	Group II	Marked
6	Group II	Marked
7	Group II	Marked
8	Group II	Marked
9	Group II	Marked
10	Group III	Marked
11	Group III	Marked
12	Group III	Moderate
13	Group IV	Marked
14	Group IV	Moderate
15	Group IV	Marked
16	Group IV	Moderate
17	Group IV	Moderate

Operation—Bilateral excision of virtually the entire great splanchnic nerve from its insertion in the celiac plexus upwards to the midthoracic level with division of all aortic branches above the diaphragm. Interruption of the communicating rami of D9, D10, D11, D12, and L1 with excision of the sympathetic trunk over this area.

In Group C cases (Table III) the same operation was done as in Group B cases, only in addition the communicating rami of L2 were divided and the ganglion itself removed on one or both sides. The immediate effect of the operation, as judged by postural change in blood pressure level, varied in the three groups. In the six cases of Group A (Table I) three showed no significant postural change, while two had a slight and one a moderate fall in systolic and diastolic levels accompanied by a fall in pulse pressure and a rise in pulse rate in the sitting and standing positions as contrasted with the lying position.

TABLE III

GROUP C

NO. CASES	STAGE OF DISEASE	POSTURAL CHANGE IN BLOOD PRESSURE
1	Group II	Profound
2	Group III	Profound
3	Group IV	Profound

Operation—Bilateral excision of virtually the entire great splanchnic nerve from its insertion in the celiac plexus to the middorsal level with division of the aortic branches. Interruption of the communicating rami of D9, D10, D11, D12, L1 with the excision of the sympathetic trunk over this area. In addition, the rami of the second lumbar ganglion were interrupted and the ganglion removed on one or both sides.

In Group B (Table II) all seventeen cases had a characteristic and definite immediate postural change. This change occurred very rapidly, in about thirty seconds after shifting position. One week after the operation was completed, the standing blood pressures were very low. As a rule, both systolic and diastolic levels were below 100 with a pulse pressure of less than 20 mm. The patient was unable to stand for more than a minute in most instances without fainting. In the course of another week, the tone of the splanchnic bed returned to some extent,

probably due to intrinsic and humoral mechanisms, so that he could begin to walk (Figure 2). By the end of three weeks, he usually was able to leave the hospital. As months passed, the postural change was less abrupt, but it usually was still present to some degree. The pulse

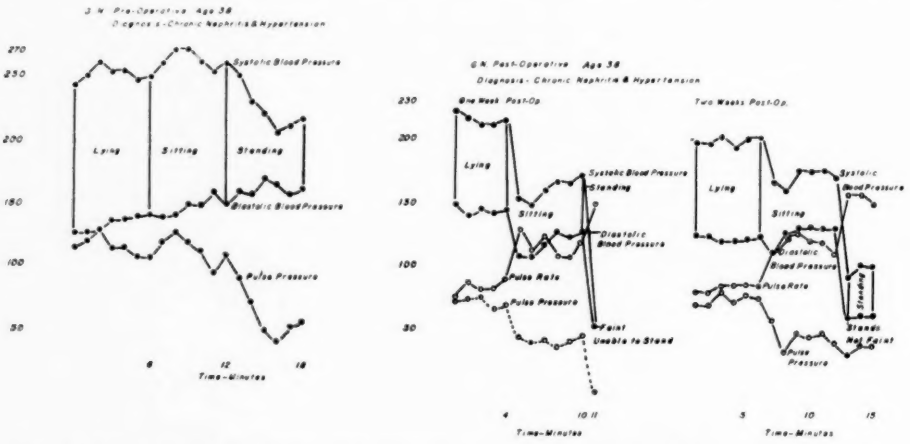

Fig. 2.—This chart shows the typical abrupt change in blood pressure, pulse pressure, and pulse rate one week after operation. The change is less marked a week later, when the standing blood pressure level is 100/60. This case happens to be a severe chronic nephritic with secondary hypertension. The character of the blood pressure change is the same as that seen after operation in primary hypertensives.

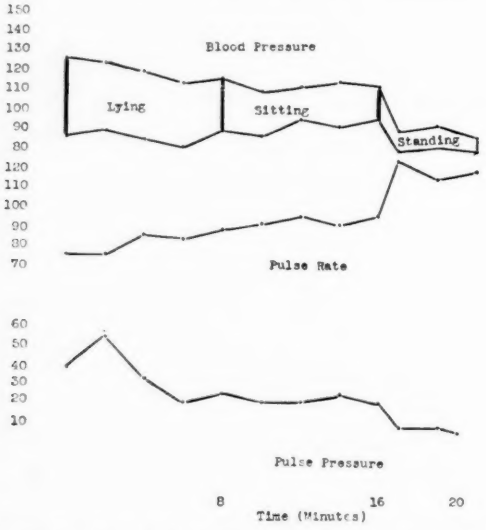

Fig. 3.—Blood pressure levels in an essential hypertensive patient (Group II) five months after operation.

pressure remained lower, and the pulse rate tended to rise as the patient shifted from the lying to the sitting and standing positions (Figs. 3, 4, 5).

In the three cases of Group C (Table III) the postural change was profound. In these the second lumbar ganglion had been removed on one or both sides in addition to what was resected in Group A and

Group B cases. It appeared to take a longer time for these patients to acquire an adequate standing blood pressure level.

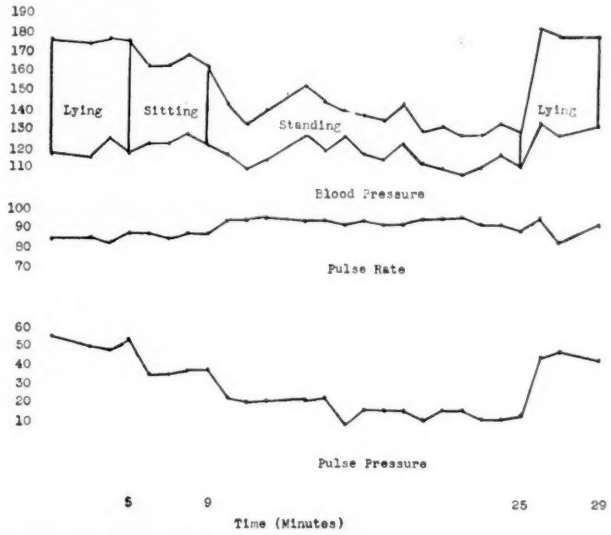

Fig. 4.—Blood pressure levels in a patient with malignant hypertension (Group IV) five months after operation.

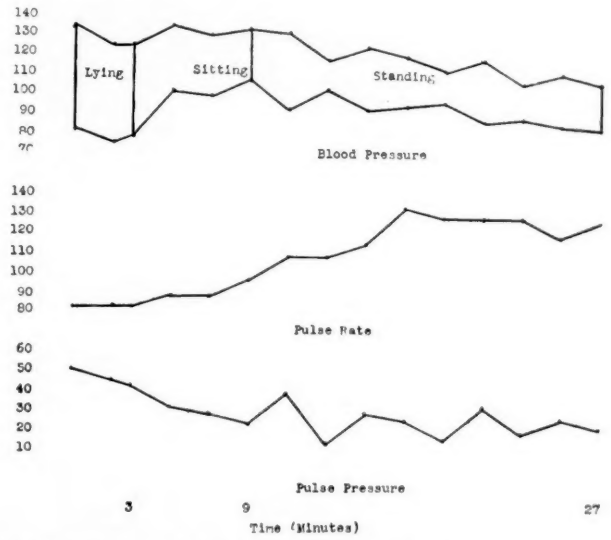

Fig. 5.—Blood pressure levels in a malignant hypertensive patient (Group IV) ten months after operation.

From these experiences, it would seem that, if the splanchnic bed is thoroughly denervated, an immediate postural change in blood pressure will result in every case. Under these circumstances the blood pressure level in all positions has been lower than before operation. The pulse pressure has been lowered in all instances. If splanchnic denervation is less complete, and no significant postural change is noted, it has been our experience that there often is no significant change

in the blood pressure level in any position, particularly in cases in the more advanced stages of the disease. Apparently, a few uninterrupted fibers are capable of supplying enough tone to the splanchnic area so that there may be no significant change in blood pressure after operation.

Removal of virtually the entire great splanchnic nerve with division of all of its aortic branches coupled with interruption of the communicating rami of D9, D10, D11, D12, and L1, together with excision of the sympathetic trunk over this area, is the minimal procedure which we have found consistently to produce a blood pressure change which is characteristic of a thorough interruption of the nerve supply to the splanchnic bed.

Whether removal of the outflow from L2 as well is necessary or desirable has not been determined as yet.

It will take several years to ascertain the value of this procedure in the treatment of hypertension in the various stages of the disease.

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THE SILK TECHNIQUE

Experimental Observations

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IT HAS been demonstrated repeatedly that a wound sutured with fine silk is less apt to suppurate than is a corresponding wound sutured with catgut.[1-3] This important consideration, coupled with the obvious advantages of silk as regards economy and reliability of sterilization, has aroused an increasing interest in "silk surgery." With the more widespread adoption of the silk technique, a number of questions have been raised regarding the proper sizes and types of silk which should be employed and regarding the technique of preparing and using the silk. It has been the purpose of the present study to attempt to answer some of these questions.

Economy of Silk.—The surgeon who has been accustomed to using catgut is likely to employ a similar technique when using silk. Thus, the silk is frequently wound on spools or small cards for sterilization and is handed to the surgeon in fairly long strands from which are made as many ties or sutures as possible in order to avoid waste. Silk is so inexpensive, however, that such efforts toward economy are entirely unnecessary, affecting as they will a saving of only a few pennies in even the most extensive operation (Table I). When the silk

Table I

Approximate Cost of Suture Material Per Operation, Showing the Great Economy in Using Silk; the Prepared Silks, Though Substantially Cheaper Than Catgut, Are More Than Twenty Times as Expensive as Untreated Silk

Amount Used	Belden Twist No. A	Champion Twist No. 3	Champion Braid No. 0	Champion "Serum-Proof" Braid No. 0	Deknatel "Moisture-Proof" Braid No. C	Chromicized Catgut No. 000
50 12-inch strands	$0.023	$0.026	$0.031	$0.48	$0.56	$1.90
100 12-inch strands	0.047	0.053	0.062	0.95	1.12	3.80
50 18-inch strands	0.037	0.04	0.046	0.70	0.85	2.87
100 18-inch strands	0.075	0.08	0.093	1.40	1.70	5.75

is prepared and used as above, the strands tend to be kinky and the technique is cumbersome. It is far more convenient to use a separate

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strand of a liberal length for each tie or stitch. If the silk is wound on a board about nine inches in length (eighteen-inch strands are handled more easily than shorter lengths), the hank of silk may be cut across at the operating table and the individual strand handed to the surgeon as it is needed (Fig. 1).

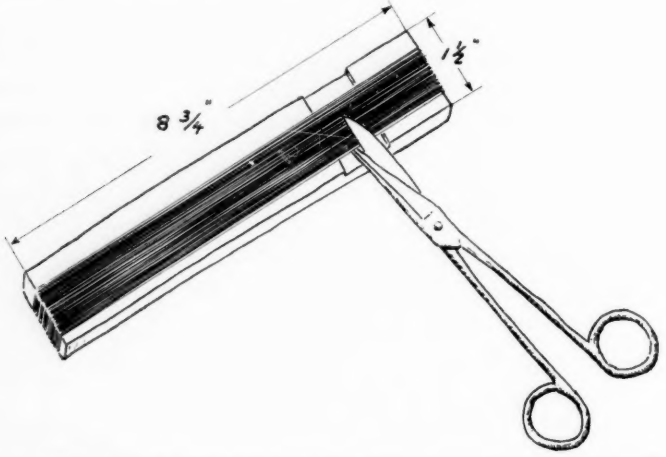

Fig. 1.—A convenient method for handling silk. Thread is wound on board before sterilization. If lubrication is desired, a small amount of vaseline, liquid petrolatum, or wax is applied to board before winding silk on it. Board then may be either boiled or autoclaved. Ends of board are smoothed to prevent fraying of silk.

Effect of Sterilization.—It has generally been held that sterilization, whether by boiling or autoclaving, weakens the silk and it has therefore been considered undesirable to prolong the period of sterilization or to use silk which has been sterilized more than once. Our observations, which accord with previous studies,[4-6] show that neither method of sterilization causes an appreciable loss of tensile strength even though the period of heating be prolonged or repeatedly applied. (Tables II, III, and IV.) Repeated boiling does increase the friability of silk, but this increase is too slight to be of clinical importance (Table V).

TABLE II

EFFECT OF REPEATED AUTOCLAVING ON THE TENSILE STRENGTH OF SILK; TESTS MADE ON DRY SILK; EACH READING IS THE AVERAGE OF TWO DETERMINATIONS

DATE	TREATMENT	CHAMPION BRAID NO. 1		CHAMPION TWIST NO. 3	
		PLAIN	"SERUM-PROOF"	PLAIN	"SERUM-PROOF"
1/ 4/38	Controls	4.25 lb.	3.58 lb.	3.6 lb.	3.4 lb.
	Autoclaved 10 min.	4.3 lb.	3.6 lb.	3.4 lb.	3.6 lb.
1/10/38	Autoclaved 10 min.				
1/11/38	Autoclaved 10 min.	4.18 lb.	3.5 lb.	3.37 lb.	3.56 lb.
1/16/38	Autoclaved 10 min.	4.31 lb.	3.75 lb.	3.43 lb.	3.43 lb.
1/17/38	Autoclaved 10 min.	4.18 lb.	3.75 lb.	3.43 lb.	3.56 lb.
1/18/38	Autoclaved 10 min.				
1/20/38	Autoclaved 10 min.	4.25 lb.	3.68 lb.	3.5 lb.	3.5 lb.

TABLE III

EFFECT OF REPEATED BOILING ON THE TENSILE STRENGTH OF SILK; TESTS MADE ON DRY SILK EXCEPT WHERE OTHERWISE INDICATED; EACH READING IS THE AVERAGE OF THREE DETERMINATIONS

DATE	TREATMENT	CHAMPION BRAID NO. 1		CHAMPION TWIST NO. 3	
		PLAIN	"SERUM-PROOF"	PLAIN	"SERUM-PROOF"
12/24/37	Controls	4.25 lb.	3.58 lb.	3.62 lb.	3.37 lb.
	Boiled 10 min.	3.31 lb. (wet)	2.75 lb. (wet)	2.56 lb. (wet)	2.68 lb. (wet)
		4.0 lb.	3.5 lb.	3.56 lb.	3.33 lb.
12/29/37	Boiled 10 min.	3.9 lb.	3.41 lb.	3.37 lb.	3.08 lb.
12/30/37	Boiled 10 min.	4.1 lb.	3.5 lb.	3.56 lb.	3.31 lb.
		3.0 lb. (wet)	2.75 lb. (wet)	2.62 lb. (wet)	2.5 lb. (wet)
1/ 4/38	Boiled 10 min.	4.25 lb.	3.62 lb.	3.56 lb.	3.37 lb.
1/ 5/38	Boiled 20 min.	4.12 lb.	3.43 lb.	3.5 lb.	3.25 lb.
1/ 7/38	Boiled 10 min.	3.93 lb.	3.18 lb.	3.25 lb.	3.12 lb.
1/ 8/38	Boiled 10 min.	4.31 lb.	3.75 lb.	3.56 lb.	3.31 lb.
		3.25 lb. (wet)	2.87 lb. (wet)	2.5 lb. (wet)	2.62 lb. (wet)

TABLE IV

EFFECT OF BOILING PERIOD ON THE TENSILE STRENGTH OF SILK; TESTS MADE ON DRY SILK

PERIOD OF BOILING	CHAMPION BRAID NO. 0	
	PLAIN	"SERUM-PROOF"
Control	2.3 lb.	3.0 lb.
5 min.	2.2 lb.	2.9 lb.
10 min.	2.0 lb.	2.8 lb.
15 min.	1.9 lb.	2.7 lb.
20 min.	2.0 lb.	2.7 lb.
30 min.	2.0 lb.	2.7 lb.

TABLE V

EFFECT OF REPEATED BOILING ON THE FRIABILITY OF SILK; TESTS MADE ON WET SUTURE TIED IN A SQUARE KNOT AROUND A CORK; SILK BOILED FOR 10 MIN. AT EACH PERIOD

NUMBER OF TIMES BOILED	NO. 3 TWIST PLAIN	NO. 3 TWIST "SERUM-PROOF"	NO. 0 BRAID PLAIN	NO. 0 BRAID "SERUM-PROOF"
(Controls)	1.9 lb.	1.6 lb.	1.6 lb.	2.0 lb.
1	1.5 lb.	1.6 lb.	1.5 lb.	1.9 lb.
2	1.6 lb.	1.6 lb.	1.5 lb.	1.8 lb.
3	1.7 lb.	1.5 lb.	1.3 lb.	1.6 lb.
4			1.3 lb.	1.7 lb.

In contrast to the resistance of silk to heat, we find that simply wetting the silk causes a prompt loss in tensile strength of about 25 per cent. This weakening effect is not caused by deteriorization because the silk regains its original strength upon drying and because it does not show a progressive loss in strength on soaking (Table VI).

The above observations hold true for braided as well as for twisted silk and for silk which has been treated with oil or wax as well as for

TABLE VI

EFFECT OF PROLONGED WETTING ON THE TENSILE STRENGTH OF SILK
(CHAMPION TWIST NO. 3)

PERIOD OF SOAKING (IN WATER)	UNTREATED	VASELINE	LIQUID PETROLATUM	WAXED	"SERUM-PROOF"
5 min.	2.3 lb.	2.9 lb.	2.7 lb.	2.2 lb.	2.4 lb.
24 hr.	2.3 lb.	2.2 lb.	2.3 lb.	2.2 lb.	2.1 lb.
7 days	2.3 lb.	2.1 lb.	2.2 lb.	2.2 lb.	2.1 lb.
14 days	2.2 lb.	2.1 lb.	2.1 lb.	2.2 lb.	2.1 lb.
21 days	2.2 lb.	2.1 lb.	2.1 lb.	2.1 lb.	2.1 lb.
28 days	2.2 lb.	2.0 lb.	2.0 lb.	2.1 lb.	2.0 lb.

untreated silk. One would think that wax or oil would protect the silk from the weakening effect of water, but such is not the case. The penetration of moisture is only delayed for a brief period by a coating of beeswax and for a slightly longer period by liquid petrolatum or vaseline (Table VII).

TABLE VII

EFFECT OF LUBRICATION AS A PROTECTION AGAINST MOISTURE
(CHAMPION TWIST NO. 3)

	TENSILE STRENGTH				
	UNTREATED	LIQUID PETROLATUM	VASELINE	WAX	"SERUM-PROOF"
Dry	3.5 lb.	3.4 lb.	3.25 lb.	3.4 lb.	3.4 lb.
Soaked 1 min.	2.5 lb.	3.1 lb.	3.0 lb.	2.6 lb.	3.31 lb.
5 min.	2.5 lb.	2.5 lb.	2.75 lb.	2.5 lb.	3.0 lb.
20 min.	2.4 lb.	2.5 lb.	2.5 lb.	2.5 lb.	2.68 lb.

Although the silk, of course, becomes moistened as it is placed in the tissues, there will be less troublesome breaking if the strands are dry when they are used. For this reason autoclaved silk will show less tendency to break than silk which has been boiled unless the latter is allowed to dry thoroughly before it is used. Oiled silk will break less easily than untreated silk because the protection against moisture, even though transitory, will allow time for the knots to be placed. Especially to be avoided, however, is the oiling of silk while it is wet because this slows up the drying process and the strands will still be weak from moisture when they are handed to the surgeon. (Table VIII.)

Lubrication of Silk.—Untreated silk has a tendency to fray and break, especially when knots are being tied under tension, and for this reason it is convenient to treat the silk with oil or wax.* This may be done at the operating table or before the silk is sterilized. The latter is preferable because excess lubrication is more easily avoided.

*The processing employed in the preparation of champion "serum-proof" silk (Gudebrod Bros.) or Deknatel's "moisture and serum-proof" silk is apparently largely an impregnation with wax. In our hands these sutures were found to show the physical characteristics of silk which has been treated with wax alone.

TABLE VIII

EFFECT OF LUBRICATION ON THE RATE OF DRYING OF WET SILK; SILK (CHAMPION NO. 3 TWIST) LUBRICATED WHILE WET AND ALLOWED TO DRY AT ROOM TEMPERATURE

	TENSILE STRENGTH		
	UNTREATED	VASELINE	WAX
Soaked 5 min.	2.75 lb.	2.68 lb.	2.5 lb.
Dried for 5 min.	3.37 lb.	2.6 lb.	2.6 lb.
Dried for 15 min.	3.4 lb.	2.75 lb.	2.9 lb.
Dried for 30 min.	3.6 lb.	2.75 lb.	
Dried for 45 min.	3.5 lb.	2.6 lb.	
Dried for 60 min.		2.7 lb.	3.4 lb.

Neither oil nor wax increases the tensile strength of the silk (Table IX). Vaseline or mineral oil makes the silk slightly less friable and prevents fraying, but the knots do not slide down smoothly. Beeswax is distinctly superior to oil in its effect on the sliding quality, but it must be appreciated that this advantage is obtained only at the expense of the stability of the knot. As will subsequently be shown, it is almost impossible to tie a reliable knot in silk which has been treated with wax alone. A combination of wax and vaseline combines the advantages of each and at the same time the sliding quality can be regulated by increasing the proportion of vaseline so that the proper type of knot will hold fairly well. It was found that approxi-

TABLE IX

EFFECT OF LUBRICATION ON THE TENSILE STRENGTH OF SILK (CHAMPION TWIST NO. 3)

	UNTREATED	LIQUID PETROLATUM	VASELINE	WAX	"SERUM-PROOF"
Dry	3.5 lb.	3.37 lb.	3.25 lb.	3.5 lb.	3.25 lb.
	3.5 lb.	3.37 lb.	3.25 lb.	3.37 lb.	3.38 lb.
	3.5 lb.	3.62 lb.	3.62 lb.	2.87 lb.	3.25 lb.
	3.3 lb.	3.62 lb.	3.63 lb.	3.13 lb.	3.11 lb.
Average	3.45 lb.	3.5 lb.	3.44 lb.	3.22 lb.	3.25 lb.
Wet (5 min.)	2.5 lb.	2.75 lb.	3.11 lb.	2.5 lb.	2.37 lb.
	2.5 lb.	3.37 lb.	3.12 lb.	2.5 lb.	2.5 lb.
	2.5 lb.	3.0 lb.	3.10 lb.	2.5 lb.	2.63 lb.
Average	2.5 lb.	3.04 lb.	3.12 lb.	2.5 lb.	2.5 lb.

mately equal parts of vaseline and beeswax melted together and allowed to harden will provide a satisfactory lubricant (Table X). An excess amount of lubricant on the silk is undesirable and it is indeed surprising how small an amount is required if it is properly applied. A convenient method is to rub a little of the mixture on both sides of the board on which the silk is to be wound. As little as 0.25 c.c. will be found sufficient for 100 turns of silk. The board is now wound, wrapped in cloth, and autoclaved.

TABLE X

EFFICIENCY OF VASELINE AND BEESWAX AS A LUBRICANT FOR SILK; THIN COATING OF LUBRICANT APPLIED TO BOARD BEFORE WINDING ON THE SILK THREAD AND AUTOCLAVING

LUBRICANT	SLIDING QUALITY	HOLDING POWER OF SQUARE KNOT	HOLDING POWER OF TRIPLE-THROW
Untreated	0	++++	++++
Vaseline	+	+++	++++
Vaseline 100 parts Beeswax 1 part	+	+++	++++
Vaseline 20 parts Beeswax 1 part	+	+++	++++
Vaseline 5 parts Beeswax 1 part	++	++	+++
Vaseline 2 parts Beeswax 1 part	++	++	+++
Vaseline 4 parts Beeswax 3 parts	+++	+	+++
Vaseline 1 part Beeswax 1 part	+++	0	+++
Vaseline 2 parts Beeswax 3 parts	+++	0	++
"Serum-proof"	+++	0	+
Beeswax	++++	0	+

The objection might be raised to lubricating the silk before sterilization that the oil and wax might protect resistant spores. The objection does not apply to this method, however, for our tests have shown that silk contaminated with the *Bacillus subtilis* and prepared as described above was uniformly sterile after autoclaving for ten minutes at fifteen pounds pressure.*

Reliability of Knots.—An important advantage of silk over catgut is the greater reliability of the knot, and it is generally assumed that a square knot in silk will not slip. Critical observation, however, shows that this cannot be accepted without certain reservations.

A simple method for testing the holding power of a knot is to tie a strand about the blades of a hemostat and observe the tendency to slip when the blades are separated. The square knot is found to be completely reliable only when untreated silk is used. When the silk has been vaselined, the square knot slips slightly but the triple-throw knot is reliable. When the silk has been waxed or "serum-proofed," a square knot slips readily and even a triple-throw knot fails to hold. (Table XI.) This is true no matter how the triple-throw knot is formed, and indeed the knot will slip even after a fourth turn has been added. Since the strength of a knot will vary somewhat according to how

*There is a real danger that oil-covered materials, such as vaselined gauze, will not be adequately sterilized by the usual methods. This is especially true if the material is in a bulky roll. Our studies have shown that such a roll of gauze one inch in diameter contaminated with *Staphylococcus aureus, Bacillus pyocyaneus,* or *Bacillus subtilis* will yield a positive culture after autoclaving for ten minutes but not after twenty minutes. We have seen pyocyaneus infections develop in clean wounds packed with vaselined gauze which had been autoclaved in rolls about two inches in diameter.

TABLE XI

HOLDING POWER OF KNOTS AS TESTED ON BLADES OF HEMOSTAT; CHAMPION SILK EXCEPT WHERE OTHERWISE STATED; ALL TESTS MADE ON WET SUTURE; THE SQUARE KNOT IS FOUND TO BE RELIABLE ONLY WITH UNTREATED SILK

TYPE OF KNOT	TWIST NO. 3 PLAIN	BRAID NO. 0 PLAIN	TWIST NO. 3 VASELINED	TWIST NO. 3 WAXED	TWIST NO. 3 "SERUM-PROOF"	BRAID NO. 0 "SERUM-PROOF"	(DEKNATEL) BRAID NO. D "MOISTURE-PROOF"
Granny	++	++	+	0	0	0	0
Square	++++	++++	+++	+	+	+	+
Surgeon's	++++	++++	++++	++	++	++	++
Triple-throw	++++	++++	++++	+++	+++	+++	+++

tightly it has been tied, tests were made with this factor controlled in a tensiometer and the results were found to be the same.

The reliability of knots was further tested, in a manner to simulate clinical conditions, by uniting strips of cloth and observing the tensile strength of the suture line. The ends were cut close to the knot (1 or 2 mm.) as is the accepted practice in the silk technique. With the untreated silk the sutures broke before the square knots untied and even the slip knots held fairly well. Vaselined silk held reliably with the triple-throw knot. Again it was observed that a completely reliable knot could not be tied with waxed or "serum-proofed" silk for with this material the knots always untied before the silk broke, even where the triple-throw knot was used. (Table XII.)

TABLE XII

RELIABILITY OF KNOTS DEMONSTRATED BY TENSILE STRENGTH OF A ROW OF FOUR INTERRUPTED SUTURES IN MUSLIN; FIGURES ARE THE AVERAGE OF SEVERAL DETERMINATIONS; WHERE "SERUM-PROOF" SILK WAS USED THE KNOTS BECAME UNTIED IN EVERY INSTANCE, EVEN WHEN THE TRIPLE-THROW KNOT WAS USED

SUTURE MATERIAL	SQUARE KNOT	GRANNY (FLAT)	GRANNY (NOT FLAT)	SLIP (SQUARE)	SLIP (GRANNY)	TRIPLE-THROW	SURGEON'S
No. 3 twist (plain)	12.8 lb.	12 lb.	11 lb.	11.0 lb.	10.5 lb.		
No. 0 braid (plain)	9.0 lb.						
No. 3 twist (vaselined)	8.0 lb.					14.0 lb.	
No. 3 twist ("serum-proof")	3.5 lb.	2 lb.		1.5 lb.	1.4 lb.	5.0 lb.	3.5 lb.
No. 0 braid ("serum-proof")	3.5 lb.					4.5 lb.	4.0 lb.
No. 2 braid ("serum-proof")	5.5 lb.						
No. 3 braid ("serum-proof")	4.0 lb.						
No. 5 braid ("serum-proof")	11.5 lb.						

The length of the cut ends is generally considered to be an important factor in the tensile strength of a knot and it has been suggested that, even in the case of silk, the ends should be left at least 3 mm. long.[7] This is contrary to the teaching of the Halsted school which insists that the sutures be cut very close to the knot so as to leave the least possible amount of suture material in the tissues. Our observations have indicated, however, that, as a general rule, a knot which is reliable will hold regardless of how short the ends are cut* and a knot which slips will continue to slip more or less indefinitely (Table XIII). Thus, with a square knot in untreated silk or a triple-throw knot

TABLE XIII

EFFECT OF THE LENGTH OF THE CUT ENDS UPON THE RELIABILITY OF THE KNOT; TENSILE STRENGTH OF A SINGLE SUTURE IN MUSLIN; FIGURES ARE THE AVERAGE OF 2:6 DETERMINATIONS

SUTURE MATERIAL	TYPE OF KNOT	LENGTH OF CUT ENDS	TENSILE STRENGTH	REMARKS
No. 3 twist (plain)	Square	½ mm.	4½ lb.	Broke
		1 mm.	4½ lb.	Broke
No. 0 braid (plain)	Square	1 mm.	3¾ lb.	Broke or untied
		2 mm.	3¼ lb.	Broke or untied
		3 mm.	3¾ lb.	Broke
No. 3 twist (vaseline)	Square	½ mm.	3½ lb.	Broke or untied
		1 mm.	4½ lb.	Broke
No. 3 twist (liquid petrolatum)	Square	1 mm.	5¾ lb.	Broke
No. 3 twist ("serum-proof")	Square	½ mm.	1 lb.	Untied
		1 mm.	1 lb.	Untied
		2 mm.	1⅛ lb.	Untied
		3 mm.	1 lb.	Untied
		1 cm.	1¼ lb.	Untied
	Triple-throw	½ mm.	2 lb.	Untied
		1 mm.	1¼ lb.	Untied
		2 mm.	2 lb.	Untied
		5 mm.	3 lb.	Broke after slipping 0.5 cm.
		1 cm.	4 lb.	Broke after slipping 0.5 cm.
No. 0 braid ("serum-proof")	Square	1 mm.	1¼ lb.	Untied
		3 mm.	1¼ lb.	Untied
		5 mm.	1¼ lb.	Untied
	Triple-throw	1 mm.	2½ lb.	Untied
		3 mm.	3¼ lb.	Untied
		5 mm.	4 lb.	Broke after slipping 3 mm.

in vaselined silk, the ends may safely be cut very close to the knot; whereas, if the silk is waxed or "serum-proofed," the knots may become untied under tension even if the ends are left 5 mm. or more in length.

Similar tests were made with catgut, for it is rather generally agreed that these knots should be safeguarded by leaving fairly long ends. It was observed that here also the length of the cut ends was of dis-

*To within 0.5 mm. in the case of fine silk.

tinctly minor importance as compared to the type of knot and type of catgut used. Square knots in plain catgut slip and become untied when the ends are cut as far as 2 cm. away from the knot and the triple-throw knot tied in chromic gut will hold even if the ends are only 2 mm. long (Table XIV). It seems apparent that one cannot

TABLE XIV

RELIABILITY OF CATGUT KNOTS AS AFFECTED BY LENGTH OF CUT ENDS; TENSILE STRENGTH OF THREE INTERRUPTED SUTURES IN MUSLIN TESTED AFTER SOAKING IN PHYSIOLOGIC SALINE SOLUTION

SUTURE MATERIAL	DURATION OF SOAK	TYPE OF KNOT	LENGTH OF CUT ENDS	TENSILE STRENGTH	REMARKS
No. 000 plain catgut (tensile strength 5¼)	1 min.	Square	1 cm.	3½ lb.	Untied
		Triple-throw	5 mm.	10 lb.	Broke
	48 hr.	Square	1 cm.	2¼ lb.	Untied
		Triple-throw	1 mm.	6 lb.	2 untied
	6 days	Square	2 cm.	3½ lb.	Untied
		Triple-throw	1 mm.	7¾ lb.	1 untied
			5 mm.	9½ lb.	Broke
			1 cm.	6½ lb.	1 untied
No. 000 chromic catgut (tensile strength 5¼)	1 min.	Square	1 mm.	10½ lb.	Broke
	48 hr.	Square	1 mm.	9¼ lb.	Broke
			2 mm.	11 lb.	Broke
			1 cm.	10½ lb.	Broke
	6 days	Square	2 mm.	9¼ lb.	Broke
		Triple-throw	2 mm.	9½ lb.	Broke
No. 0 plain catgut (tensile strength 10)	2 hr.	Square	2 mm.	2 lb.	Untied
			3 mm.	2¼ lb.	Untied
			1 cm.	1 lb.	Untied
		Triple-throw	2 mm.	13 lb.	Broke
No. 0 chromic catgut (tensile strength 9½)	2 hr.	Square	3 mm.	2 lb.	Untied
			1 cm.	2 lb.	Untied
		Triple-throw	3 mm.	14 lb.	Broke
No. 3 silk twist (tensile strength 2½)	48 hr.	Square	1 mm.	13½ lb.	Broke
	6 days	Square	1 mm.	12½ lb.	Broke
No. 3 twist ("serum-proof")	6 days	Triple-throw	1 mm.	8¾ lb.	2 untied

depend upon long ends to protect the knot, but rather that one should employ a type of knot which is reliable for the particular suture material used. Suture material should be avoided where the most reliable of the surgical knots, the triple-throw knot, fails to hold. Even if knots could be relied upon to tighten and hold after slipping for a certain distance, accurate approximation of the tissues would be lost and the surgeon's technique would thereby lose precision. These observations with catgut lead us to the conclusion that the triple-throw knot should always be employed for plain catgut and for the larger sizes of chromic catgut; whereas, for the smaller sizes of chromic gut the square knot may be relied upon. In either case there is little advantage in leaving the cut ends longer than 2 or 3 mm.

To return to silk, it is interesting to note that with the twisted silk knots appear to hold better than with the braided. The "surgeon's knot" shows little superiority over the ordinary square knot as regards the holding power of the knot, but it has the advantage, which may in certain circumstances be very important, that the first throw will stay in place without maintaining tension on the suture. This permits the accurate placing of ties on delicate and friable tissues.

Size of Suture.—Published descriptions of the silk technique generally advise the use of "fine silk," but all too often the exact sizes are not stated. Moreover, the various manufacturers employ widely different scales of size terminology so that, unless the brand and type of silk are specified, the size number or letter is meaningless (Table XV). This has led many surgeons who are adopting the silk technique to employ silk which is unnecessarily heavy, a practice which may lead to trouble if the wound suppurates.

TABLE XV

SHOWING THE COMPLETE LACK OF UNIFORMITY IN THE SIZE TERMINOLOGY OF SUTURE MATERIALS

APPROXIMATE DIAMETER	APPROXIMATE TENSILE STRENGTH	BELDEN TWIST	CHAMPION		DEKNATEL	CATGUT
			TWIST	BRAID		
0.0025 in.	½ lb.			000 000	A	
0.003 in.	1½ lb.		1	00	B	
0.005 in.	3 lb.	A	3	0	C	000 00
0.007 in.	3½ lb.		4	1	D	
0.008 in.	4 lb.			2		
0.009 in.	4½ lb.	C	6	3	1	000
0.010 in.	5 lb.	D	7	4		
0.011 in.	8 lb.		10	5		00
0.012 in.				6	2	
0.013 in.	10 lb.		13	7		0
0.015 in.				8	3	1
0.018 in.	12 lb.			9	4	2
0.021 in.	16 lb.			12	5	3
0.023 in.	20 lb.			18	6	4
0.027 in.	30 lb.			19	7	5

The strength of suture material to be employed should logically depend upon the holding power of the tissue into which the suture is placed. Howes and Harvey[8] have pointed out that nothing is gained by using a suture with a tensile strength greater than the holding power of the tissue. This does not mean, however, that the tensile strength of the suture material should be the same as the holding power of the tissue, because a single interrupted stitch uniting the tissues consists of two strands between the tissues. On the other hand, the strength of the stitch is not twice that of a single strand, because one of the two strands contains the knot which, because of shearing

action, is weaker than the intact strand. Tests show that the strength of a silk stitch is about 75 per cent greater than the tensile strength of a single strand of the silk.

With catgut we must allow for the progressive loss of tensile strength of the suture in the tissues.[8] Since this does not have to be considered in the case of silk, at least during the early period of wound repair when the strength of the stitches is an important factor, we may conclude that the proper size of suture is one with a tensile strength only 55 to 60 per cent of the holding power of the tissue.

In our hands the holding power of the various tissues has proved to be considerably less than was found by Howes and Harvey (Table XVI). According to our tests, a silk thread with a tensile strength

TABLE XVI

HOLDING POWER OF THE VARIOUS TISSUES AS TESTED BY A SINGLE SUTURE OF NO. 3 SILK TWIST (TENSILE STRENGTH OF THIS STITCH IS 4½ LB.)

TISSUE	DOG	HUMAN
Anterior rectus sheath (as in longitudinal incision)	4 lb.	2¼ lb.
Anterior rectus sheath (as in transverse incision)	4½ lb.	2½ lb.
Rectus muscle (as in longitudinal incision)	2 lb.	
Rectus muscle (as in transverse incision)	2 lb.	1¼ lb.
Median nerve (stitch placed in epineurium)		1½ lb.
Wrist tendon (stitch placed in epitenon)	⅞ lb.	⅞ lb.
Peritoneum and transverse fascia		1¼ lb.
Posterior rectus sheath (upper abdomen)		1 lb.
Posterior sheath with peritoneum and transversalis fascia (upper abdomen)	1¼ lb.	
Subcutaneous fat	1 lb.	
Subcutaneous fat with superficial fascia	2½ lb.	
Small bowel		
Serosa	½ lb.	
Serosa and submucosa	⅞ lb.	
All layers	⅞ lb.	

of only one and one-fourth pounds (i.e., champion twist No. 0) should be strong enough even for fascial stitches because the strength of the stitch itself is two and one-fourth pounds. For practical purposes, however, silk as fine as this is difficult to use because it breaks too readily on tying. Therefore, as routine material for sutures and hemostatic ties a strand about 0.005 inch in diameter with a tensile strength of approximately three pounds is recommended (Table XV). The only occasion for using heavier silk would be for mass ligatures, which are to be avoided, or for pulling together structures which cannot easily be approximated. In the latter instance the fate of the suture line would still be dubious, however, because the constant tension would cause the stitches gradually to cut through.* It might seem that larger sizes would show less tendency to cut through the tissue. Our tests, however, in agreement with the findings of Howes and Harvey,

*Mason and Shearon[9] found that tendons sutured with silk separated about one inch even when the limb was fixed in a position of relaxation, apparently due to the constant slight muscle pull.

show that this is not the case. A No. 13 silk twist with a diameter of 0.013 inch tears through tissue at the same pull as does a No. 0 twist with a diameter of only 0.003 inch.

Technique of Suturing.—How close together should the stitches be placed in a suture line? Howes and Harvey considered this problem briefly in their studies with catgut and concluded that "little strength is gained by multiplying the number of interrupted sutures in a given area." This would seem theoretically to be rather surprising because the strength of a suture line depends upon two factors, the holding power of the tissue and the strength of the stitches, and both of these factors are directly affected by the number of stitches in a given area.

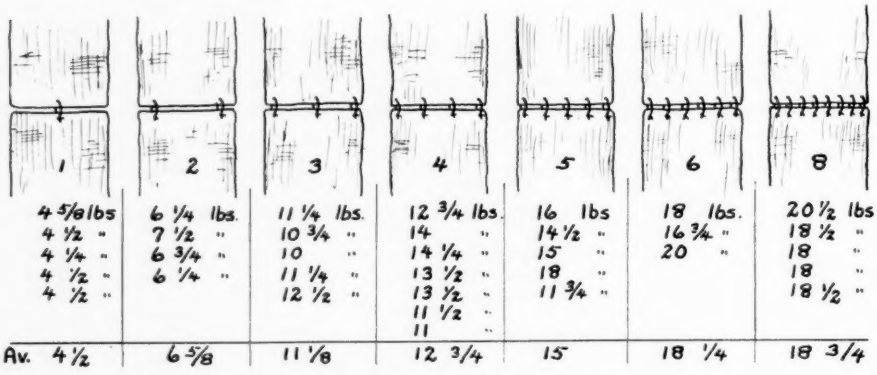

Fig. 2.—Effect of multiplication of sutures on strength of suture line, where suture is weaker than tissue. Interrupted sutures of champion twist No. 3 (untreated, wet, tensile strength 2⅝ lb.) placed in muslin.

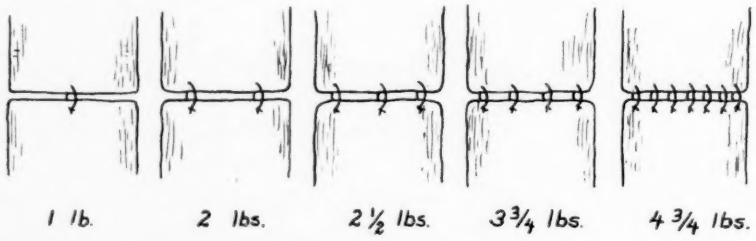

Fig. 3.—Effect of multiplication of sutures on strength of suture line, where suture is stronger than tissue. Interrupted stitches of champion twist No. 0 (untreated, wet, tensile strength 1¼ lb.) placed in weak cloth.

The strength of the suture line does not increase in mathematical proportion with an increase in the number of stitches, probably because the strain is not evenly distributed, but certainly a great increase in strength is gained (Figs. 2 and 3). There is a further advantage in placing a relatively large number of stitches in that a more accurate approximation is attained. This is especially important where the tissues are brought together under a certain amount of tension or where there is likely to be tension during the process of repair. Thus the optimum frequency of stitches depends upon the number required

for accurate approximation and upon the strength required of the suture line, for, as has been shown, the strength of the suture line can be increased only by increasing the number of stitches and not by employing heavier suture material. The number of stitches indicated will, therefore, vary widely according to the circumstances. In some instances they will best be placed only a few millimeters apart.

These observations apply to a continuous suture as well. A continuous suture is stronger than a row of interrupted sutures with a corresponding number of stitches because there are only two knots to weaken the structure and because the tension is more evenly distributed among the individual bites. There are, however, the obvious disadvantages that a defect and break in the strand will forfeit the whole suture line and that the larger single piece of foreign material may, in case of suppuration, cause more trouble than would the smaller fragments.

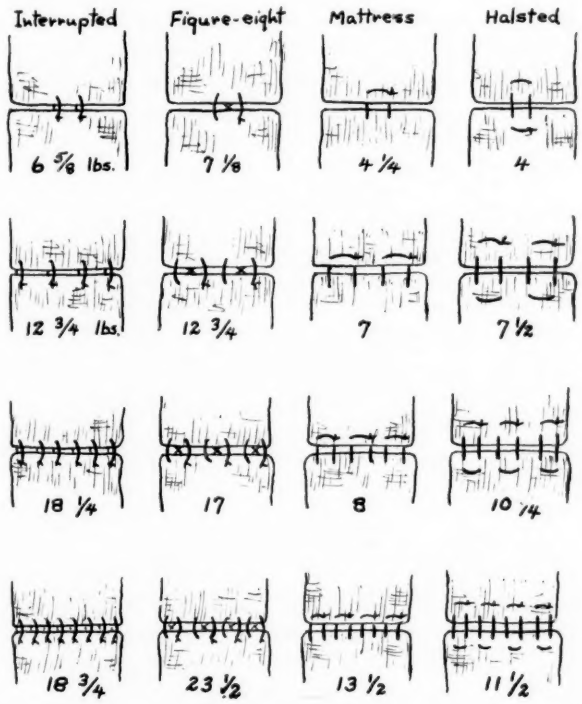

Fig. 4.—Holding power of the various stitches, where suture is weaker than tissue (champion twist No. 3 placed in muslin).

What are the relative merits of the various types of stitches? To answer this question we must consider separately two factors: the strength of the suture material and the holding power of the tissue. Where the holding power of the tissue is relatively great, a figure-of-eight stitch shows approximately the same strength as two simple stitches because in either case the tissues are united by four strands of suture. Since there is only one knot in the figure-of-eight, however,

one would expect a slightly greater tensile strength and such indeed proves to be the case, although the difference is not important. The mattress stitch is weaker than the figure-of-eight because there are only two strands uniting the tissues and accordingly it is no stronger than a single simple stitch. (Fig. 4.) On the other hand, when we are dealing with tissue with poor holding power, we find that the number of strands uniting the tissues is not as important as the number of points where the tissue is engaged by the stitch. In this case, therefore, the mattress stitch is stronger than a simple stitch but neither the mattress nor the figure-of-eight has any advantage over two simple stitches. (Fig. 5.) The mattress and Halsted types of stitches have special advantages in obtaining a wider area of contact between the tissues, and so, of course, have their definite indications, but, as far as the strength of the suture line is concerned, a row of simple interrupted stitches is just as satisfactory as a series of figure-of-eight stitches and is definitely superior to a series of mattress stitches.

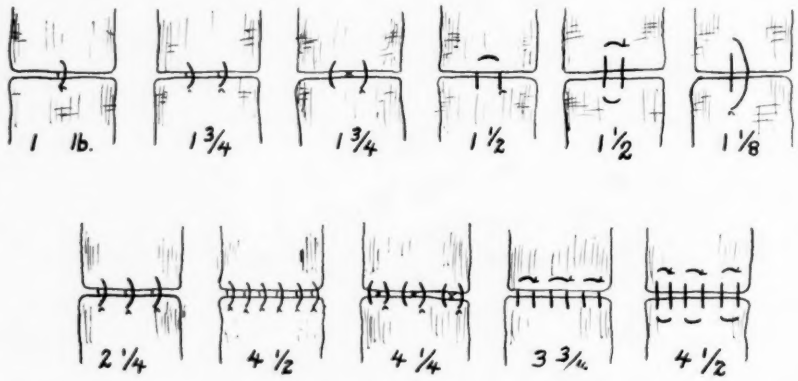

Fig. 5.—Holding power of the various stitches, where suture is stronger than the tissue (champion twist No. 3 placed in rotted cotton cloth).

CONCLUSIONS

1. Silk is not weakened by sterilization but loses strength by about one-fourth when it is wet. Autoclaving is therefore preferable to boiling since the silk is dry when used.

2. The square knot is reliable only in the case of untreated silk.

3. Lubrication is usually desirable to prevent fraying and breaking, especially where knots must be tied under tension.

4. Oiling with vaseline or mineral oil prevents fraying, but the knots do not slide down perfectly.

5. Treatment with beeswax gives ideal lubrication but only at the expense of the holding power of the knot.

6. A reliable knot cannot be tied in silk which has been treated with wax alone; even the triple-throw knot fails to hold.

7. A satisfactory lubricant is a mixture of wax and vaseline which is best applied by smearing a small amount on the board on which

the silk is subsequently wound. As the silk is autoclaved, the lubricant distributes itself evenly over the strands.

8. Bacteriologic tests show that silk thus prepared is reliably sterile.

9. With silk treated in this manner, the square knot is not reliable, but the triple-throw knot will hold satisfactorily.

10. Fine silk (diameter, 0.005 inch; tensile strength, three pounds) is amply strong for routine use, including fascial suturing.

11. Increased strength in the suture line may be obtained not by employing heavier suture material but by increasing the number of individual stitches in a given area.

12. A suture line of simple interrupted stitches is approximately as strong as one of figure-of-eight stitches and stronger than one of mattress stitches.

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THE IMMEDIATE STRENGTH OF THE SUTURED WOUND*†

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THIS paper is an attempt to explain the degree of strength which can be given to the repair of a wound by means of sutures.

The common belief is that the strength of the sutured wound is dependent on the thread strength of the sutures employed to hold the tissues together. Actually, the number of sutures employed is a contributing factor, but the holding power of the tissue really determines the strength of the union and the strength of the sutures in the wound is much less than generally supposed. For example, when sutures are placed in a wound, they lose strength both by wetting with tissue fluids and by knotting. By wetting they lose about 30 per cent of their original dry-thread strength. Catgut with a dry-thread strength of 21 pounds decreases to 15 pounds, while silk with a dry-thread strength of 3.1 pounds decreases to 2.2 pounds. Linen does not lose strength by wetting alone, but when boiled five minutes, and then wet, linen also loses 30 per cent of dry-thread strength. Knotting causes a loss of 40 to 50 per cent of dry-thread strength, while wetting and knotting cause a loss of approximately 50 to 60 per cent. The residual or functionating strength is, therefore, only about 40 or 50 per cent of the original dry-thread strength (Table I) and unfortunately this residual or functionating strength is not always proportional to original dry-thread strength. Thus, the functionating strengths of Nos. 2 and 3 catguts are not proportional to the dry-thread strengths (Table I) and are in fact no greater than functionating strength of No. 1. For silk the functionating strengths are somewhat more proportional to the dry-thread strengths, but still the loss of strength which all kinds of sutures sustain by insertion into the wound is of such magnitude that the residual strengths do not have the supposed advantages indicated by the original dry-thread strengths. The entire range of strength for the different sizes is contracted and the variations between the sizes reduced in amount. For instance, the functionating strengths of the different sizes of catgut No. 00 to No. 3 vary only from 2 to 8.51 pounds, or a difference of 6.5 pounds for the entire range; while the dry-thread strengths extend from 5.7 to 23 pounds, a range of 17.3 pounds. With silk the functionating strengths vary only from 1.7 to 4.9 pounds from Nos. A to E, a difference of 3 pounds, while the dry strengths range from 3 to 8.4 pounds, or a difference of 5½ pounds. Because of this contraction in the range of strength and because of the lack

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TABLE I

BREAKING STRENGTH AFTER WETTING AND KNOTTING CATGUT AND SILK POUNDS

	Catgut					
SIZES	NO. 000	NO. 00	NO. 0	NO. 1	NO. 2	NO. 3
Dry Normal—pounds	Avg., 5.7	Avg., 6.2	Avg., 10.9	Avg., 17.0	Avg., 18.3	Avg., 23.9
Wet (30 min.) Knotted Tested wet	Avg., 2.3	Avg., 2.5	Avg., 4.3	Avg., 7.3	Avg., 7.1	Avg., 6.3
Wet (2 hr.) Knotted Tested wet		Avg., 2.2	Avg., 4.2	Avg., 8.5	Avg., 8.5	Avg., 8.1
Percentage of original strength		36	35	50	35	35

	*Silk**					
SIZES	NO. 000	NO. 00	NO. 0	NO. A	NO. C	NO. E
Dry Normal	Avg., 3.3	Avg., 6.0	Avg., 8.4	Avg., 3.5	Avg., 4.5	Avg., 8.0
Wet (30 min.) Knotted	Avg., 1.7	Avg., 3.5	Avg., 4.0	Avg., 2.0	Avg., 2.0	Avg., 4.4
Percentage of original strength	51	58	47	57	60	55

*The gradation of silk according to sizes is very confusing. Some manufacturers indicate sizes by letters, some employ a gradation corresponding to catgut sizes, while others have an absolutely unrelated system. Throughout the text of this article, the size of catgut is usually quoted and any gradation of silk may be applied when the strength corresponds.

of proportion to the dry-thread strengths, the functionating strength of a suture is a better guide to the usefulness of that suture than the dry-thread strength.

The principal reason, however, why the strength of the sutured wound is not dependent on strength of the sutures used is because the holding powers of tissues for the sutures are, in most instances, less than the functionating strengths of the sutures and the holding powers are not in any way influenced by the thread strengths of the sutures employed. The holding powers of tissues were determined in the following manner: The tissue to be investigated was secured in one clamp of a tensile strength machine and the stitch inserted about 0.5 cm. deep into its substance in such a way that the suture had to be pulled out at right angles to the direction of the fibers of the tissue. The free ends of the stitch were placed in the other clamp of the machine to obtain the necessary traction. In this way the holding power of the tissues was compared with the dry-thread strengths of the different sizes of sutures. The constancy of the amount of holding power possessed by each tissue regardless of the size of the suture used is illustrated in Table II. Muscle had a holding power of 2.8 pounds, regardless of whether size No. 3 or size No. 00 catgut was used; while fascia had a holding power of 8.3 pounds with size No. 0 or

any larger suture. Fascia,* as would be expected, possessed the greatest amount of holding power, while fat had the least. On the other hand, when the stitch was pulled out parallel to the fibers of the tissues, holding power fell markedly; that for fascia diminished to 2 pounds, for example, while that for muscle was almost negligible. It should be noted, however, that the tendinous inscriptions of muscles have a holding power similar to fascia.

TABLE II

HOLDING POWER OF TISSUES FOR DIFFERENT SIZE OF CATGUT*

TISSUE†	SIZE OF SUTURE	AVERAGE DRY TENSILE STRENGTH (POUNDS)	HOLDING POWER (POUNDS)
Fat	00	6.2	0.4
	0	10.0	0.6
	1	16.0	0.5
	2	18.3	0.3
	3	23.9	0.4
		Average	0.44
Peritoneum postsheath	00		2.3
	0		2.3
	1		1.8
	2		2.0
	3		1.8
			1.9
Muscle	00		3.0
	0		3.0
	1		2.8
	2		2.6
	3		3.0
			2.8
Fascia	00		Suture broke, no test
	0		8.2
	1		9.0
	2		7.8
	3		8.1
			8.3

*In all tests except one, the tissue tore, signifying that the strengths obtained were holding powers.

†Same structure, i.e., particular muscle or fascia, used in each test. When different fasciae were used, holding powers varied from 3 to 8.5 pounds. There is very little variability in holding powers of different muscles except in tendinous inscriptions.

It would seem, therefore, that the capacity of a tissue to hold a suture is determined by the component of fibrous tissue present in that tissue, its density, and the manner in which the suture pulls against the architectural arrangement and not by the strength of the suture used unless this strength is less than the holding power of the tissue. Fat has a loose and sparse component of fibrous connective tissue and little holding power, while fascia is dense fibrous tissue and has a large amount of holding power, providing, of course, the sutures pull at right angles to the fibers. In the repair of wounds the sutures frequently have to pull

*When all tissues are included and not just soft tissues, drilled bone and ligamentous structures exceed fascia in holding-power strengths.

parallel to the tissue fibers and unfortunately such unions are weak, regardless of the strength of the sutures used. For example, the sutured union of the posterior sheath of the rectus muscle in the repair of the longitudinal incision in the anterior abdominal wall never can be made as strong as the repair of the anterior sheath, regardless of the strength of the sutures used. In the posterior sheath, the fibers in general run transversely, and the sutures pull out parallel to them; while in the anterior sheath the fibers mostly run longitudinally and the sutures pull at right angles to them. In the same way the full holding power of tendon can never be entirely utilized, because, in spite of the ingenious types of sutures which have been devised, they all pull out more or less parallel to the collagenous bundles of the tendon.

In Table III the functionating strengths of the various sizes of sutures are compared to the holding powers of the various tissues. In the last column is the determinant of the strength of the union, based on whether the functionating strength of the suture is greater or less than the holding power of that particular tissue. It will be noted that in all tissues except fascia the strength of the union is determined by holding power of the tissues and that this strength is less than the functionating strength of the sutures usually employed, beginning with size No. 00. In fascia,

TABLE III

COMPARISON OF HOLDING POWER AND FUNCTIONATING STRENGTH OF SUTURES (SINGLE BITE)

TISSUES	AVERAGE HOLDING POWER	FUNCTIONATING STRENGTHS, SINGLE SUTURE		DETERMINATION OF STRENGTH OF UNION
		Catgut	*Silk*	
Fat	0.44 lb.	00-2.2	00-3.5	Holding power
		0 -4.2	0 -4.0	Holding power
		1 -8.5		Holding power
		2 -8.5		Holding power
		3 -8.5		Holding power
Peritoneum and post-sheath	1.9 lb.	00-2.2	00-3.5	Holding power
		0 -4.2	0 -4.0	Holding power
		1 -8.5		Holding power
		2 -8.5		Holding power
		3 -8.5		Holding power
Muscle	2.8 lb.	00-2.2	00-3.5	Suture*
		0 -4.2	0 -4.0	Holding power
		1 -8.5		Holding power
		2 -8.5		Holding power
		3 -8.5		Holding power
Fascia	3-8.3 lb.	00-2.2	00-3.5	Suture*
		0 -4.2	0 -4.0	Suture*
		1 -8.5		Holding power
		2 -8.5		Holding power
		3 -8.5		Holding power
		4 -8.5		Holding power

*See text for determinant when multiple sutures are used.

however, the holding power exceeds the functionating strength of size No. 0; but, again, when the suture pulls parallel to its fibers, the functionating strength of No. 00 is greater. In every instance, therefore, except in fascia, the tissues hold the sutures and not the sutures the tissues, and the corollary is equally as true, that the strength of the wound can never be greater than the holding power of tissues for the sutures. A crude simile will perhaps illustrate the situation: two pieces of cheese cloth cannot be sewed together any more securely with rope than with thread, for the flimsy mesh of the cloth has no greater holding power for the larger and stronger strand than for the smaller one. Even in fascia, holding power definitely limits the strength of the sutured union when a suture of sufficient functionating strength is employed. In this tissue it is only with the finest sizes Nos. 000 and 00 that the limiting strength set by holding power is reduced by insufficient functionating strength, and actually this does not happen when the relationship of holding power to functionating strength is considered for multiple sutures.

The degree to which holding power is increased by using many sutures has been studied as follows: A constant length of abdominal wall of the rabbit, skin not included, was secured with an increasing number of sutures possessing excessive functionating strength in the single stitch and the strength of the union determined by pulling the edges apart. Each suture was placed 1 cm. deep. The tissues tore each time, indicating the strengths obtained were those of holding power. Table IV shows that the holding power for two stitches is not double that for one, but that an increment of strength is added by each additional suture until a maximum strength is reached with a concentration of sutures approximately 0.5 cm. apart. Additional holding power was not obtained by placing the sutures closer together. On the other hand, the functionating strength of two sutures was double that of one, four of two, etc. Now, considering that holding power does not increase in direct proportion to the number of sutures used, while functionating strength does, it is obvious that the ratio of functionating strength to holding power constantly increases as each suture is added to the wound. To state the circumstances in another way, the tension or strain which must be overcome to hold the wound edges together is divided into smaller portions as the number of sutures is increased and the stress thrown onto each one of the sutures becomes less with the addition of every new one. Moreover, there is apparently no limit to the division which can be obtained by increasing the number of sutures, while holding power soon reaches a maximum with a definite concentration of sutures. Holding power, therefore, becomes more and more of a limiting factor when many sutures are used and yet, when many sutures are used, less strength is required of each one. For this reason, there is little danger of reducing the maximum strength of the union set by the holding power of fascia by using a

suture of insufficient functionating strength, providing, of course, that an adequate number of sutures is used.

TABLE IV

INCREASE OF HOLDING POWER (*A*) AND FUNCTIONAL STRENGTH (*B*) BY INCREASING THE NUMBER OF SUTURES USED

A. 1 interrupted suture, No. E silk in fascia equals 3.0 lb.
2 interrupted sutures, No. E silk in fascia equals 3.9 lb.
3 interrupted sutures, No. E silk in fascia equals 5.0 lb.
8 interrupted sutures, No. E silk in fascia equals 9.0 lb.
8 interrupted sutures, No. C silk in fascia equals 9.0 lb.
8 interrupted sutures, No. A silk in fascia equals 8.5 lb.

B. Knotted, size No. 0 catgut
1 strand equals 4.1 lb.
2 strands equal 8.0 lb.
3 strands equal 12.0 lb., etc.

Again it will be noted in Table IV that the holding power of the tissue is not influenced by the strength of sutures used even when they are multiple. Eight large silk sutures (No. E) contributed no more strength to the sutured union than eight fine sutures (No. A) with a functionating strength less than the holding power of the tissue.

The question whether a stronger closure of the wound results from the use of a continuous suture or from the use of interrupted sutures has also been considered. In the last analysis the continuous variety is only another form of multiple sutures, so all the arguments just used for the relationship of functionating strength to holding power apply; namely, that the holding power is the limiting factor. However, it might be argued that the continuous variety suffers less loss of strength than the interrupted variety, because there are fewer knots in it in proportion to the number of bites of tissue and knotting causes the loss of thread strength. The relative strength of the two types was therefore estimated in the following manner: An equal length of the skin of the dog which has an excessive amount of holding power was closed, in one instance, with a number of interrupted sutures of fine size and next by a continuous suture of the same size with a number of loops corresponding to the number of interrupted sutures. Thus, a continuous suture of four loops and two knots was compared to four interrupted sutures with four knots and a continuous suture of six loops and two knots was compared with six interrupted sutures and six knots (Table V). The results failed to show that the strength of the repair sutured with the continuous variety was in any way superior to the closure with interrupted sutures. The explanation is quite simple. In the continuous variety the entire tension is divided between the strands and finally distributed to the weakest knot which disrupts, and, in the case of the interrupted sutures, the tension is distributed between the same number of strands and again the weakest knot breaks. The skin, as was pointed out, is ex-

ceptionally strong and forced the sutures to tear in these special tests. In most instances the tissue itself would have torn.

From another viewpoint though, interrupted sutures have a distinct advantage over a continuous type. If during the healing of the wound the knot of the continuous variety breaks or the strand itself disintegrates or the holding power of the tissues for one loop is destroyed in any one place, then the whole integrity of the union is threatened. With interrupted sutures, on the other hand, each suture is a separate unit of strength and if the integrity of one is lost the others carry on their intended functions.

The extent of the bite of the suture or the depth to which it is inserted into the tissue naturally influences the amount of holding power of that tissue, but only in those which possess a fair degree of holding power for a bite of any depth. In fascia, for example, a bite of 1 cm. has a holding power of 5 pounds, while in the same fascia a bite of 0.5 cm. has a holding power of 7 pounds. In muscle and fat, to the contrary, an increase of the bite to the same depth contributed only a negligible increase in strength. This increase of strength with the larger bite in fascia is without advantage, moreover, for the larger bite leaves behind an un-

TABLE V*

INTERRUPTED SUTURES		CONTINUOUS SUTURES	
No. 4—4 knots	13.0 lb.	4 loops	7.2 lb.
	10.0 lb.	2 knots	16.0 lb.
	17.5 lb.		16.5 lb.
	13.5 lb.		10.0 lb.
Average	13.0 lb.		12.1 lb.
No. 6—6 knots	19.0 lb.	6 loops	23.5 lb.
	14.5 lb.		7.0 lb.
	15.0 lb.	2 knots	11.0 lb.
	15.3 lb.		14.0 lb.
Average	15.8 lb.		13.8 lb.

*No. 00 catgut used throughout. Sutures broke in all tests.

necessary amount of suture material or foreign body in the wound without a remarkable gain in strength. With the employment of the larger bite, also, there is a tendency to tie the sutures tighter causing strangulation of the tissue and necrosis.

Last, there are certain features in the actual suturing of the wound clinically which cannot be evaluated mechanically from the suturing of two detached pieces of dead flesh. In the wound part of the strain preventing separation of the edges is born by the intact and uninjured tissues at either end of the defect. More important still, the tissues about the wound are living and tend to splint the area of separation during the first few days of healing and to contract and lessen the size of the defect and the tension across it in the later days of the repair. The vitality of the tissue maintains the holding power of the tissue, and, in fact, it is

impossible to preserve the continuity of cut edges for any considerable length of time when tissue death or atrophy of tissue occurs. It is absolutely essential, therefore, even from the point of view of the strength of the repair that the method of suturing preserves the viability of the tissues, and, of course, it is absolutely necessary for obtaining satisfactory wound healing.

In conclusion, as far as strength is concerned, and this discussion has been entirely devoted to strength, there is no need of suturing any other tissue but fascia, except to eliminate dead space or in the case of the peritoneum to prevent herniation. Moreover, when multiple sutures are used, there is no need to use a suture with a functional strength stronger than No. 0 catgut, because the holding-power strengths of all tissues are less and really limit the strength of the repair. The use of any larger suture simply provides an excess amount of foreign material, no greater strength, and presents the possibility of untoward wound healing. Increasing the number of sutures employed increases the amount of holding power of the tissues, but, more important still, increases in direct proportion the functionating strength of the sutures, providing a better ratio of functionating strength of holding power. Less strain is, therefore, thrown on each suture. Increasing the bite of tissue enhances holding power to a slight degree, but only in fascia. The danger of tissue necrosis is so great with the use of the deep-bite suture that it should only be used sparingly, and better healing is usually obtained when it is not used. When sutures are going to pull out parallel to the fibers of the tissues, the repair will be weak and special attention must be given to increasing the holding power of these tissues either by using mattress sutures or by constructing the wound in such a manner that the fibers will not be cut across. Incisions of the exterior abdominal wall which split the fibers and do not cut them recently have been advocated again by Singleton.[2] Interrupted sutures are recommended because the strength of each unit is preserved when the suture material is being absorbed or holding power lost in one portion of a wound and not because they give greater strength than the continuous suture. Under similar conditions the integrity of continuous suture would be entirely lost.

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THE REACTION OF EXPERIMENTAL SARCOMAS TO THE WOUND-HEALING STIMULUS*

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PREVIOUS experimental work dealing with the possible relationship between chronic inflammation and carcinogenesis has been summarized in a recent paper by Brunschwig, Tschetter, and Bissell. The reported results have been conflicting in that in some instances chronic inflammation was thought to reinforce experimental carcinogenesis by tar; whereas, in other instances it was felt that this was not the case. The above authors observed that the wound-healing stimulus, as afforded by the creation of large ulcers with radium or the actual cautery, when applied to cutaneous epithelium which was exposed to a carcinogenic compound did not under experimental conditions hasten the formation of epidermoid carcinoma. In a more recent publication Beck observed that the appearance of sarcomas in the subcutaneous tissues of the rats was not hastened when the carcinogenic compound was injected with turpentine, the latter inducing a severe inflammatory reaction about the injected agent.

The following experiments were performed to observe whether in experimental sarcomas the addition of the wound-healing stimulus would result in an increase in the growth rate in the region of the tumors where such stimulus was applied.

Methods.—Sarcomas in the subcutaneous tissues of the backs of rats were induced by the injection of 1 to 2 mg. of methylcholanthrene suspended in 0.1 to 0.2 c.c. of lard. When the tumors appeared three to seven months after injection, they were exposed through a cutaneous incision over them, and an elongated wedge-shaped piece of the neoplasm, 2.5 to 3 cm. long and 0.7 cm. deep, was removed by sharp dissection (Fig. 1). The edges of the trough-like wound thus made in the tumor were not approximated but remained separated for a distance of about 1 cm.; the skin incision was then closed by interrupted silk sutures. The tumors varied in size when they were operated upon and the portion removed extended almost from one pole of the oval mass to the other in the smaller neoplasms, but in the moderate-sized neoplasms the length of the wound corresponded to only a segment of the total circumference of the growth. In two in-

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stances biopsies were made from the wound sites approximately five days after operation, and the cutaneous incisions again closed.

The animals died or were killed at varying intervals following the operation. A study of the gross contour of the neoplasms was made with reference to any bulges in the regions where the wounds were made or to other evidence that the neoplastic tissue was proliferating or infiltrating surrounding normal tissues at a greater rate in these regions than elsewhere. Oblong blocks of tissue were taken at right angles to the long axes of the wounds for microscopic study, after death of the animals.

Eighteen neoplasms were operated upon, with three immediate deaths, leaving fifteen for study. The latter died or were killed from one to thirty-five days after operation. Seven survived the operation twenty to thirty-five days.

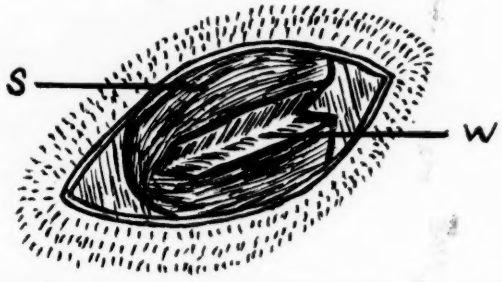

Fig. 1.—Diagrammatic illustration to show manner of making wedge-shaped wounds in experimental sarcomas. *S*, Sarcoma of subcutaneous tissue produced by injection of methylcholanthrene; *W*, wedge-shaped wound in the neoplasm.

The gross findings may be summarized as follows (Figs. 2 and 3):

1. Obliteration of the trough-like wounds occurred in approximately twelve to fourteen days by what was essentially proliferation of tissue from the wound surfaces in the tumor. There was little evidence to indicate that any appreciable healing occurred as the result of invasion by surrounding nonneoplastic tissue.

2. In some instances where the wounds had healed it was difficult to ascertain exactly the previous site of the wound.

3. A study of the entire excised tumor masses showed no evidence in any case that there was stimulation of growth in the region of the experimental wounds. These regions showed no bulges as compared with other surfaces of the tumor. In fact, where the wound region did not conform in general to the contour of the whole tumor, it presented a cicatrix which was puckered and slightly depressed below the surrounding surfaces.

4. Areas of spontaneous degeneration are very often observed in experimental sarcomas and in some cases here studied such spontaneous necrosis of tumor tissue and overlying skin occurred, but not necessarily in wound areas. In two instances such degeneration did occur

in the wound areas; in one case the skin and subjacent wound area became necrotic and in another case a large cystic space containing yellowish fluid developed at the wound site.

5. Measurements of the tumor were made just before operation and at death of the animal. While growth rates of the tumors varied, all of them increased gradually in size following operation. From previous experience with sarcomas produced in the manner herein described, it was the impression that no undue rapidity in growth of the whole tumor occurred after operation.

Fig. 2.—Showing large sarcoma on back of rat thirty-one days after wound was made through healed incision. Sutures had remained in the wound for purposes of marking. Note smooth symmetrical contour of the tumor mass with no bulge of tissue in the wound area.

Histologically the sarcomas were essentially fibro- or spindle-cell sarcomas of various types, with varying amounts of collagen.

Microscopic examinations of sections made transversely to the long axes of the wounds as described above may be summarized as follows:

1. By the fifth or sixth day following the operation, the tumor tissue constituting the wound edges is edematous, and there are many dilated capillaries. Spindle-shaped cells are observed to extend toward the wound at right angles to the wound surface. They have an immature appearance, but it is not possible to state whether they are

true tumor cells or are immature fibroblasts arising from nonneoplastic elements of the stroma of the tumor which were stimulated to proliferation by the making of the wound. At least both neoplastic and nonneoplastic elements were taking part in this repair. The capillaries appeared to be true capillaries and not vascular spaces in buds of tumor cells.

2. By the eleventh to seventeenth day the wounds were for the most part closed and an irregular cicatricial area at the surface was present which included spindle cells that may or may not be neoplastic, frequently separated by broad bundles of collagen (not very dense). Bordering this cicatrix the tumor tissue did not appear to differ greatly from that elsewhere in the neoplasm. In some instances irregular areas of "coagulation necrosis," including "shadows" of spindle cells, were present. Edematous and necrotic tissue detritis was present over the wound sites and beneath the overlying skin.

Fig. 3.—Showing excised tumor thirty-one days after operation. *S*, Reflected skin over wound site which has healed and is represented as a puckered scar, *W*; *B*, block of tissue removed to obtain sections transversely through wound site for microscopic study.

3. Sections from tumor sites twenty to thirty-five days after operation showed essentially the same as above with perhaps a diminution of the cicatrix area. Because in these larger growths increasing numbers of areas of spontaneous degeneration occurred, it was more difficult to discern with certainty what was previously the wound area.

DISCUSSION

Normal tissue in a relatively resting state, when subjected to mechanical trauma such as obtains when a wound is made with loss of tissue, exhibits a series of proliferative changes that occur in a more or less orderly manner, the object of which is to restore, to some extent at least, the removed tissue and to restore structural continuity. In the above studies, wounds with loss of tissue were made in soft parts sarcomas which are, of course, composed of cells that are already proliferating unrestrained by the factors which govern normal tissue growth, differentiation, and maintenance. It was observed that these wounds healed over a period of days and that, while the tumor mass was increasing in size, the superposition of the wound-healing stimulus in a given region did not result in excess stimulation of growth in these regions as compared with uninjured portions of the neoplasms. In fact, the general contour of the expanding tumor mass was maintained, and, if this was locally slightly distorted, it was in the form of a slightly depressed or puckered scar rather than a localized bulge in the mass.

While it is perhaps not possible to draw conclusions in regard to the biology of human sarcomas from the experiments reviewed above, a practical clinical inference that is suggested is that trauma to a malignant neoplasm, such as obtains when biopsy is performed, does not in itself necessarily constitute a stimulus to increased growth of the neoplasm. Where clinical observations seem to indicate that biopsy was followed by increased rate of spread, it would appear that this might be the result of seeding of tumor cells in surrounding tissue during such a procedure. The question of increasing the likelihood of metastases is another problem since this brings up the possibility of forcing tumor cells into vascular channels by an operative procedure carried out within neoplastic tissue.

SUMMARY

Wounds with loss of substance, produced in experimental soft parts sarcomas, healed in what appeared to be an orderly fashion while the tumor mass as a whole increased in size. The contour of the healing and healed portions of the sarcoma conformed to the contour of the growing tumor mass. No localized increase in growth due to the wound-healing stimulus superimposed upon the already present proliferative stimuli within the malignant cells was noted. The repair of the wounds in the neoplasms was accomplished by proliferation of cells of the tumor mass and not by ingrowth of nonneoplastic tissue from the immediate vicinity about the tumor.

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AN EXPERIMENTAL STUDY OF THE BACTERIOLOGY OF PERFORATION PERITONITIS*

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THE study of the bacteriology of peritonitis resulting from perforation of the intestinal tract has been undertaken more or less casually for a good many years, mainly by physicians and surgeons to round out the study of particular cases of this condition. But there has been much disagreement regarding the roles of the different organisms, and particularly of the certain organism, if any, which is the primary cause of the infection, and there has been little systematic investigation.

The interrelationships of the many species of bacteria in the intestinal tract are very complex. It seems unlikely that these relationships are maintained when the organisms escape into the peritoneal cavity. It has been noted that fewer species of bacteria are found in peritoneal infections than would be expected if the effect were due to a simple maintenance of the intestinal relationships after the organisms have escaped into the peritoneal cavity. The groups of organisms which survive under these conditions are quite well known, and, of these, the colon bacillus and the streptococci are the ones most commonly mentioned.

In the work under discussion, an experimental study of the subject was undertaken, the object being to discover, if possible, which intestinal organism or organisms play the primary role in establishing the infection. But, as the experiments progressed and, especially, as the colon bacillus thrust itself into greater prominence in the results, the aspects of the problem changed and other angles of the subject were investigated.

In the studies of perforation peritonitis which have been previously reported, the colon bacillus and the streptococcus have been the organisms most commonly noted, and opinion is somewhat divided as to which is the more important in establishing the infection. Pawlowsky[16] injected intestinal contents intraperitoneally into animals and found that many of the animals died; if he first sterilized the intestinal contents, few died. From this he concluded that the cause of perforation peritonitis was bacterial. Malvoz[11] thought, from a study of many cases of this condition, that *Escherichia coli* was the sole cause. Brütt,[2] Dudgeon and Mitchiner,[5] Warren,[21] and McClure and Altemeier[12] found *E. coli* to be the predominating organism in appendicitis and in the

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peritonitis resulting from perforation of the appendix. Streptococci were found to be common, but less so than coliform organisms. Theobald Smith[18] injected guinea pigs intraperitoneally with pure cultures of coliform organisms isolated from "scours" in calves and found that the animals developed a peritonitis which was often quickly fatal. Altemeier[1] reviewed the literature on the bacteriology of perforation peritonitis and presented a study of 100 cases of his own. He found that those cases which yielded a mixed flora were by far the most severe.

The object of the work here reported has been to discover, if possible, which of the intestinal organisms play the primary role in establishing perforation peritonitis. A total of twenty-six suspensions of cecal contents were injected into 40 guinea pigs, 16 rabbits, and 6 white mice. The suspensions of the cecal contents were prepared by adding approximately 10 c.c. of the cecal contents to approximately 20 c.c. of sterile physiologic saline solution. The larger particles were allowed to settle out by gravity and the supernatant liquid was injected intraperitoneally into the experimental animals. Guinea pigs received approximately 5 c.c. apiece, rabbits 10 c.c., and mice 1 c.c. The cecal contents were obtained from normal animals killed in the course of other experiments or from the human cecum at autopsy. In 12 more guinea pigs the peritonitis was produced by laparotomy and incision of the cecum, in order to approximate more closely the conditions obtained in actual perforation peritonitis. Of these 12 animals, 7, or 58 per cent, died of the infection, a percentage only slightly higher than that found among the animals inoculated with cecal contents by means of a syringe; and, since the laparotomy method was no more certain and seemed to involve factors of shock and local injury, this method was not used further. In 3 of the experiments the animals were injected with human cecal contents, and in 5 experiments with samples from rabbits; in the other 18 the cecal contents of guinea pigs were used.

The cecal flora of a normal guinea pig, as seen under the microscope, is extremely complex. Short gram-negative rods of the morphologic types of the colon typhoid group are nearly always seen but occasionally are sparse and difficult to find. Spore-bearing rods are universal and numerous. Microscopically many different types can be found: large, medium, and small; clostridial, square, and long slender types; square, pointed, or rounded ends; equatorial, terminal, or subterminal spores; and chained, paired, or single forms. Other gram-positive rods of many shapes and sizes are also rather numerous, but much less so than the spore-bearing group. In the guinea pig cecum a multitude of spiral forms, long or short, thick, or thin, with single or multiple curves, can be seen. Some are spirilla, but the majority are spirochetes, and these forms are usually so numerous as to outnumber all of the other forms. Fusiform organisms of varying sizes are common and fairly numerous. Cocci are usually few in numbers; streptococci are most easily found,

but diplococci and single forms sometimes can be found after some searching. Yeasts, algae, and fine-branched filaments occur rarely. Animal parasites are also occasionally seen, usually protozoa of the class Mastigophora, especially trichomonas. The microscopic picture of the samples used here showed the typical intestinal flora of the animals from which they were taken. Leucocytes from the animal were fairly common and in one case there was definite phagocytosis of the intestinal organisms.

After the injections, the cecal contents were planted on media, including 1:10 rabbit blood nutrient agar, and slides were made for examination for the types of organisms mentioned above. The inoculated media were examined for hemolysis after incubation, and different types of colonies were picked. Coliform organisms were kept for further study. However, since the cecal flora of a guinea pig is so very complex and since a large number of the types of organisms which make up this flora will not grow upon aerobic plates of the type used, the proportions of the aerobic organisms found upon these plates, especially of the coliform organisms and of the various types of spore-formers, are misleading, and do not in any way represent the true proportions of these organisms in the cecal contents.

The injected animals were autopsied as soon as they died, and, in some cases, if they survived for four days, they were killed and autopsied. It was found that after four days few animals died and autopsies performed after this time revealed few or no changes in the organs and cultures yielded few or no bacteria. The peritoneal fluids of the autopsied animals were inoculated onto the same media as were used for the suspensions, and slides of the fluids were made. The organs were examined and pieces were taken for microscopic study.

Animals injected with cecal suspensions (or operated as described) do not always die. Of the 74 animals treated, 33, or 46 per cent, died. This death rate varied very slightly with the species of animal injected and with the species of animal used as the source of the sample.

Early in the experiments, two very interesting features were noted. The first was the regularity with which organisms of the coliform group were isolated from the peritoneal fluids of the animals which died of the injections. These microorganisms were isolated from 51 per cent of all of the 57 animals which were autopsied and from 84 per cent of the 33 animals which died in four days; while they were isolated from only 16 per cent of the 24 animals which survived and were killed and autopsied.

Streptococci were very seldom found either in the original samples or in the peritoneal fluids of the injected animals. Careful examination of the original smears and of smears of the cultures revealed these organisms in 17 per cent of the suspensions and in 19 per cent of the animals. Attempts to procure pure cultures of the streptococci were

unsuccessful. On several occasions, however, mixed cultures of streptococci and coliform organisms were injected intraperitoneally into guinea pigs, and cultures of the peritoneal fluids of the 5 animals which died showed that the streptococci were very infrequent or had died out entirely, while the coliform organisms were abundant. Other organisms (staphylococci, diptheroids, spore-formers, etc.), of course, were common in the suspensions and in the peritoneal fluids of the animals which died shortly after the injections, but were rarely found in the later stages of the infection; if they exerted any effect on the course of the peritonitis, this must have been at the very beginning.

A second feature noted was the low death rate among animals injected with cecal samples from which no members of the coliform group could be isolated by the routine method. It is generally believed by bacteriologists that colon bacilli are constant parasites of the large intestines of all warm-blooded animals. Chapman and Lieb,[4] however, found that the numbers of *E. coli* in the intestines were in indirect proportion to the severity of the obscure intestinal conditions which they were studying, and that the presence of pathogenic staphylococci in the nose and throat and of pathogenic streptococci in the intestines inhibited the colon bacilli in the intestines. Therefore, they thought that the presence of many colon bacilli in the intestines was normal and that the staphylococci and streptococci play an important role in these conditions by their inhibitive action. In this work, as a general rule, members of the coliform group were so numerous in the samples that the routine method seldom failed to reveal a large preponderance of these organisms over all other types in the cultures isolated. But, at times, certain lots of guinea pigs were received, from which cultures of the suspensions showed few or no members of this group and even further searching failed to detect them. The dominant organisms in the samples seemed to be more or less constant in each lot; for example, the first lot yielded large numbers of *Pseudomonas aeruginosa*, an organism only occasionally found in the rest of the experiments; the second and third lots, staphylococci; the fourth, spore-formers; and the fifth, an orange diphtheroid. No explanation of this phenomenon has been sought, but it is an interesting and noteworthy observation that certain lots of guinea pigs have too few coliform organisms in their cecums to be detected by culture.

But the significance of this observation, from the point of view of the subject studied here, lay in the fact that few of the animals injected with samples in which coliform organisms were scarce died of the injections (10, or 33 per cent, of the 30 animals, as compared with 64 per cent of the 44 animals injected with samples in which coliform organisms were abundant). With six of the ten samples in these lots, none of the 12 animals died. From the 10 animals which did die of the injections of the other samples of this type, coliform organisms could usually

be recovered, except from the 6 animals which died from injections of the samples containing many pseudomonas. It would seem that these animals were susceptible to the few coliform organisms in the material injected. At any rate, this is clear evidence that without coliform organisms the cecal contents are not likely to give rise to a fatal peritonitis.

The symptoms, autopsy findings, and tissues of the injected animals which died showed only those features to be expected in acute peritonitis. In those animals which survived, the main findings were organization of the exudate and adhesions. The adhesions showed a tendency to localize the infection in an area of the peritoneum. This was especially notable in the laparotomized animals which survived, as the adhesions completely plugged the incisions in the cecums and walled off the infections.

Microscopic examination of the exudates indicated that organisms other than streptococci and coliform organisms disappeared rapidly, probably through the combined action of phagocytosis and lysis. It was noted that gram-positive organisms were phagocytized more extensively than the gram-negative rods, and that, as the infection proceeded, the microbial flora became continuously simpler. It was often observed in the smears that nonphagocytized organisms appeared to be swollen and pale-staining. This was interpreted as evidence of extracellular lysis, but it was impossible to make quantitative observations of this phenomenon or to determine precisely the types of organisms which were being dissolved. However, since the spiral organisms, as a rule, disappeared before phagocytosis had begun, it would seem that these forms are disposed of by lysis and the spore-formers and other gram-positive types by phagocytosis later.

The cultures of the peritoneal fluids of the 61 autopsied animals, including some injected with the washings of the peritoneal cavities of animals injected with the samples, yielded pure cultures of coliform organisms in 13, or 21 per cent. This group included the animals injected with the peritoneal washings. In 11, or 18 per cent, few organisms other than members of the coliform group were isolated. In 7, or 11 per cent, a fairly large number of spore-formers were found, and in 6, or 10 per cent, a number of staphylococci in addition to coliform organisms. These were all animals which died in about eighteen hours after the injections. In 4, or 7 per cent, a number of streptococci were seen in the cultures. Twelve, or 20 per cent, all of which survived or had been injected with samples containing no coliform organisms, yielded no coliform organisms on culture; and 9, or 15 per cent, all of which had survived, gave completely negative cultures.

Having established the importance of the coliform group in the development and course of perforation peritonitis, experiments were carried out to see if the introduction of pure cultures of members of this group into the peritoneal cavity would give rise to conditions in the

injected animals similar to those resulting from the introduction of the total cecal flora. During the course of the investigation, guinea pigs were frequently injected intraperitoneally with suspensions in physiologic saline solution of freshly isolated coliform organisms in order to test the pathogenicity of the strains. The death rate from the injections was rather high; thirty, or 70 per cent, of the forty-three strains tested killed the test guinea pigs. This may be due to the rather large dose employed. It was found experimentally that 2 c.c. of a suspension of an eighteen-hour agar slant in 10 c.c. of physiologic saline solution was the best rough estimate of pathogenicity. Whether the organisms came directly from the cecal contents or from the peritoneal fluid of an injected animal seemed to have little effect upon the mortality of the guinea pigs. The findings at autopsy and the smears of the peritoneal fluids of these animals resembled closely those of the animals injected with the total cecal contents.

The peritoneal cavities of some of the guinea pigs injected with the suspensions were washed with sterile saline solution and the washings injected intraperitoneally into normal guinea pigs. Of 4 guinea pigs injected with washings from animals dead of the original injections, 3 died, and the findings at autopsy were noteworthy because of the selection of the coliform organisms by this process. In one case streptococci, which were seen in the fluids of the first animals, died out and the peritoneal fluids of the second animals yielded an abundance of coliform organisms.

Another experiment was suggested by the observation that a few of the guinea pigs, when injected with the cecal samples, showed immediate, though temporary, signs of illness. Okada,[15] studying experimental perforation peritonitis in dogs, thought that histamine was one of the most important causative factors in this condition. To test the possibility of this having some bearing on the results found in this work, guinea pigs were injected, one with a filtrate of a cecal suspension, one with a suspension in the filtrate of a coliform organism, and one with a saline suspension of the same organism. The filtrate-injected animal survived; the other two died. This was considered indicative of the absence of a noncellular toxic substance in the filtrate.

Steinberg and Ecker[20] report the finding of a soluble substance from cultures of *E. coli* which was toxic for rabbits. One of the cultures used in the work reported here, when heat-killed and injected intravenously into rabbits, killed many of them with toxic symptoms. To test the possibility of such a toxic substance in the culture, rabbits were injected intravenously with filtrates of broth cultures and of saline suspensions of agar slant cultures and with unheated living cultures of this organism. The rabbits survived and showed no symptoms. It was, therefore, concluded that heating the culture formed some toxic substance not present in the filtrate or in the living culture.

An attempt was made to classify the strains obtained, to see if there were any bases by which the pathogenic could be distinguished from the nonpathogenic members. The question of the pathogenicity of the coliform group has been the subject of much discussion, the general opinion being that they are seldom very active pathogens. It is well known that coliform organisms are the most common cause of ascending infections of the urinary tract. There are scattered case reports of meningitis and septicemia in newborn children caused by colon bacilli. The work of Theobald Smith[18] has established that "scours" in calves is due to pathogenic strains of *E. coli*. Smith and Little[18] found experimentally that strains from this source were definitely pathogenic for many species of animals. But throughout bacteriologic literature one finds the tacit assumption that very few strains of *E. coli* are pathogenic and that infections with this organism are rare.

The classification of the colon-aerogenes group on the basis of cultural characters has been subjected to much investigation, which is still in progress and far from being settled. At the present time it seems to be generally conceded that members of the group fluctuate about two modal types, which are designated as Escherichia and Aerobacter respectively. But there also occur many intermediate forms. Members of the genus Escherichia are often subdivided into the species communis, not fermenting sucrose, and communior, which does ferment this sugar. Members of the genus Aerobacter are identified by the production of acetylmethylcarbinol and the power to attack citrate. Members of the whole group which correspond in some characters to one genus and in others to the other are termed intermediates.

The subject of hemolysis in the coliform group and its relationship to pathogenicity and to cultural reactions has received much attention. Schmidt[17] could not correlate hemolysis with any other character. Dudgeon, Wordley, and Bawtree[7] found that if one colony in a urinary infection was hemolytic the rest were also, while fecal strains were about equally divided between hemolytic and nonhemolytic strains. The hemolytic strains slowly lost the power to dissolve blood cells on storage, but the nonhemolytic strains did not gain it. Herrold[8] also found that the hemolytic property was a constant character of the strains in which it was found, but he could not correlate it with any other property of the strains. Nickolls[14] found hemolytic strains from patients with ulcerative colitis to be more virulent for mice than hemolytic strains from normal individuals. Buchgraber and Hilko[3] found a definite, but not absolute, correlation between hemolysis and the fermentation of sucrose.

The various pure cultures which I have studied behaved much alike, whether they came from cecal contents or from peritoneal exudates, or from animals of the same or another species, when tested for pathogenicity. Of the 11 rabbit strains tested, 61 per cent were pathogenic for test guinea pigs; of the 6 human strains, 61 per cent; of the 17 strains

isolated from injected guinea pigs, 62 per cent were pathogenic. From this it can be seen that many strains of coliform organisms, picked at random from a group, are pathogenic for guinea pigs when injected intraperitoneally. There was little difference noted when the strains were divided by cultural reactions, since of the 18 *E. coli communior* and 21 *E. coli communis* strains tested, about 60 per cent of each were pathogenic. The Aerobacter and intermediate types were much less frequently pathogenic, but these types were also far less numerous. Of the 18 hemolytic strains tested, 10, or 56 per cent, were pathogenic as compared to 9, or 82 per cent, of the 11 nonhemolytic strains. Of the 60 sucrose-positive members of the *E. coli* group tested for hemolysis, 30, or 50 per cent, were hemolytic; while 12, or 22 per cent, of the 55 sucrose-negative members of this group were hemolytic. The intermediate group tested (15 strains) had 9, or 61 per cent, which were hemolytic. But this correlation is not definite enough for any relationship to be established.

The serologic relationships of the coliform group, and even of members of the same species in the group, are very confused. Mackie[10] and Dudgeon, Wordley, and Bawtree[7] found little or no cross agglutination between strains of the group. Herrold[8] and Dudgeon and Pulvertaft[6] found agglutinins and precipitins to be type specific for the hemolytic strains but not for the nonhemolytic strains. Meyer and Löwenberg[13] found that hemolytic strains fell into a serologically united group with cross agglutinations; the nonhemolytic strains were only agglutinated by homologous antisera, but some sera against nonhemolytic strains agglutinated some of the hemolytic group. Nickolls[14] found that strains of hemolytic *E. coli* from normal feces and from feces of patients with ulcerative colitis were heterogeneous with occasional cross agglutinations. Lovell[9] found little cross agglutination between strains and often only low titers against the homologous antisera. It would seem from the published work that within the species *E. coli* there are many serologic subtypes.

The two antisera used in these experiments were prepared by repeatedly injecting rabbits intravenously with strains isolated during the experiments. One strain was isolated from the peritoneal cavity of a guinea pig which had died from an injection of the cecal contents of a guinea pig; the other was isolated directly from the cecal contents of a rabbit. Both strains were of the *E. coli communior* type, hemolytic, and pathogenic for guinea pigs.

The majority (57 per cent) of the 131 strains of coliform organisms tested against these antisera were agglutinated by neither of the sera. Of the 51 strains isolated from guinea pigs, 27, or 53 per cent, were agglutinated by the guinea pig antiserum and 23, or 45 per cent, were agglutinated by neither antiserum. The guinea pig antiserum agglutinated 53, or 40 per cent, of all the strains tested and the rabbit anti-

serum only 29, or 22 per cent; and, as a general rule, the strains agglutinated by the rabbit antiserum were also agglutinated by the guinea pig antiserum. When the strains were divided by cultural reactions, 36, or 55 per cent, of the 64 *E. coli communior* strains (the type to which both of the immunization cultures belonged) were agglutinated by either or both of the antisera; while only 13, or 19 per cent, of the 68 *E. coli communis* strains were agglutinated and 9, or 56 per cent, of the 16 strains of other types tested. Of the 49 hemolytic strains tested, 35, or 71 per cent, were agglutinated; while only 14, or 25 per cent, of the 57 nonhemolytic strains were agglutinated. When the cultures were grouped by the individual sources from which they originated, it was seen that, even there, there was little agreement as to the serologic reactions of the strains.

CONCLUSIONS

Guinea pigs, rabbits, and white mice were inoculated with the total cecal contents of guinea pigs, rabbits, and human beings. Of the organisms of the cecum which may escape into the peritoneal cavity on perforation, the coliform group are those most likely to cause peritonitis. Members of this group were the only intestinal bacteria found to be consistently pathogenic. The samples of the cecal contents containing few or no coliform organisms rarely gave rise to peritonitis. A large proportion of strains of colon bacilli occurring in the intestines are potentially virulent. Pathogenic strains of the coliform group cannot be distinguished by cultural characters, hemolysis, agglutinations, or any combination of these characters from the nonpathogenic strains.

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TRAUMA AND APPENDICITIS

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DURING the past few years, there have appeared in the literature a number of articles under the heading "Traumatic Appendicitis." Some of the cases presented are rather convincing, but in the majority the evidence in favor of trauma's playing a part in the etiology is rather flimsy, to say the least. Several authors state that the majority of the medical profession consider traumatic appendicitis a definite entity. I could find nothing in the literature upon which they based such an assertion. Therefore, I sent questionnaires to 125 leading surgeons in all parts of the United States, with the hope of obtaining data which would be of value in determining their reaction upon the subject. Eighty-seven surgeons responded. A few did not wish to be quoted, and the answers of two were too vague to be of value. The names and opinions of eighty-one are outlined in Table I.

The men quoted operated upon more than 72,803 cases of acute appendicitis. All agree that trauma, as an etiologic factor in acute appendicitis, is rare. Thirty-one, or 37.27 per cent, feel that it is possible for trauma to cause appendicitis. Six, or 7.4 per cent, believe that a previously diseased appendix might be aggravated by trauma but that appendicitis could not be initiated by an injury. Only eleven, or 13.58 per cent, think that a strain can play any part in the etiology of appendicitis. Twenty-four, or 29.62 per cent, saw cases in which they believed trauma entered into the etiology.

Questionnaires were also sent to 100 hospitals in the various sections of our country. Thirty hospitals answered, and the results are tabulated in Table II. There were 49,604 cases of acute appendicitis reported, with a history of trauma in only eleven. In one a pin was found in the appendix, and another was a case of intussusception, without external violence. If these two are eliminated, the remaining nine cases would give a percentage of 0.0018 in which trauma was mentioned as an etiologic agent.

The term, traumatic appendicitis, as used in this paper, refers only to appendicitis caused by external violence or muscular strain.

In the earlier articles the authors spoke of traumatic aggravation of a pre-existing chronic appendicitis, and this was explained by direct injury to the appendix or its mesentery. The explanation given in the more recent literature is one of overdistention of the appendical lumen by cecal contents as the result of increased intra-abdominal pressure.

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TABLE I

SURGEONS	DO YOU BELIEVE THAT TRAUMATIC APPENDICITIS IS A DEFINITE ENTITY?	CAN APPENDICITIS BE PRODUCED BY A STRAIN?	HAVE YOU EVER SEEN A CASE CAUSED BY TRAUMA?	NUMBER OF CASES OPERATED IN THE PAST TEN YEARS
Clark L. Abbott, Oakland, Calif.	I believe that it could be.	I believe that any condition of strain which produces internal colon pressure may be a causative factor.	No	Did not state
Irvin Abell, Jr., Louisville, Ky.	No	No	No	500
Robert J. Alexander, Salt Lake City, Utah	No	No	No	More than 900
Elmer R. Arn, Dayton, Ohio	No	No	No	3,516
W. Wayne Babcock, Philadelphia, Pa.	Possible by injury comparable to that leading to crush or rupture of the intestine.	No	Have seen a few cases where quiescent appendix has been lighted into activity by trauma.	2,000 or 3,000
Fred Bailey, St. Louis, Mo.	I do not believe a normal appendix could be sufficiently traumatized by a nonpenetrating injury to cause acute appendicitis.	No	One. A case of subacute appendicitis directly traumatized and it progressed into gangrene and rupture.	Probably 300 or over
Fredric W. Bancroft, New York, N. Y.	Yes	No, unless under some unusual condition.	No	Several hundred
Robert F. Barber, Brooklyn, N. Y.	No	No	No	Perhaps 2,000 to 3,000
Fenwick Beekman, New York, N. Y.	Might be possible for trauma to cause obstruction to the circulation, producing appendicitis. Must be rare.	No	No	200
Bertram Bernheim, Baltimore, Md.	No	No	No	Several hundred

R. Russell Best, Omaha, Neb.	Possible, but must be rare.	No	No	400
Carl E. Black, Jacksonville, Ill.	Possible, but rare.	Strain would have to be severe enough to amount to trauma.	No	About 250
John O. Bower, Philadelphia, Pa.	No	No	No	Did not state
James A. Cahill, Jr., Washington, D. C.	No	No	No	About 3,500
V. E. Chesky, Halstead, Kan.	No	No	I saw one case where an oil-field worker claimed to have been struck in the abdomen three days before. The appendix was ruptured when he entered our hospital.	About 400
Reynold Church, New York, N. Y.	No	No	No	More than 500
W. A. Coventry, Duluth, Minn.	No	No	No	More than 500
Wm. A. Cubbins, Chicago, Ill.	I think there is only one time to make a diagnosis of traumatic appendicitis, and that is when a perfectly well individual gives a history of having had a severe abdominal injury, is operated upon early, and a microscopic section shows an injury to tissues. This could not possibly be demonstrated after a lapse of twenty-four hours.	I have had only one case in my experience where there was any possibility of stating that a strain had anything to do with the production of an acute appendicitis.	A wrestler who ate a heavy meal at noon engaged in a heavy wrestling struggle at 4 o'clock and immediately afterward suffered severe pain, agonizing in type. He was operated upon about four hours later, and microscopic section showed he had apparently ruptured the inner lining of his appendix.	About 250

TABLE I—CONT'D

SURGEONS	DO YOU BELIEVE THAT TRAUMATIC APPENDICITIS IS A DEFINITE ENTITY?	CAN APPENDICITIS BE PRODUCED BY A STRAIN?	HAVE YOU EVER SEEN A CASE CAUSED BY TRAUMA?	NUMBER OF CASES OPERATED IN THE PAST TEN YEARS
George M. Curtis, Columbus, Ohio	Theoretically possible.	Theoretically possible.	No	323
Vernon C. David, Chicago, Ill.	No	No	No	Did not state
Edward B. Dewey, Pasadena, Calif.	Yes. Rare.	No	One. Result of jumping six feet to ground. Symptoms followed immediately. At operation, fecalith with obstruction and beginning gangrene was found.	Did not state
Arthur W. Elting, Albany, N. Y.	No	No	No	Did not state
W. L. Estes, Jr., Bethlehem, Pa.	No	No	Have seen one case of acute suppurative appendicitis, in which I thought trauma might have something to do with its etiology.	2,500
John M. T. Finney, Baltimore, Md.	Yes	Yes	Yes	2,000 conservative estimate
John M. T. Finney, Jr., Baltimore, Md.	Yes, but exceedingly rare.	It is conceivable that it could be caused by a strain.	Two. A child 6 years old fell from a porch (about five feet) and struck flat on abdomen. Operated upon within six hours. A very acute appendicitis was found. I also saw a case where a revolver bullet perforated the appendix.	About 2,000

Joseph H. Fobes, New York, N. Y.	No	No	No	At least 500
Joseph H. Francis, Memphis, Tenn.	No	No	No	300 to 500
Louis Frank, Louisville, Ky.	No	No	No	At least 500 or 600
W. Edward Gallie, Toronto, Ont.	I think it is possible that blows on the abdomen might distend an appendix and so induce an inflammatory reaction.	I expect it could result from sudden increase of intra-abdominal pressure.	No	Few in last ten years, but several hundred before that.
Gatewood, Chicago, Ill.	Theoretically possible.	No	No	463
Willis D. Gatch, Indianapolis, Ind.	Possible for a direct blow over an inflamed or an adherent appendix to cause trouble.	No	No	Easily 1,000
C. F. Hegner, Denver, Colo.	Per se, no. May be contributory in a previously diseased appendix.	No	No	120
Arthur E. Hertzler, Halstead, Kan.	No	No	No	500 to 1,000
Charles G. Heyd, New York, N. Y.	No	No	No	691
Wm. B. Holden, Portland, Ore.	If so very rare.	No	No	500 to 1,000
J. Shelton Horsley, Richmond, Va.	Yes	No	I do not recall a case in which the diagnosis was unquestionable.	My two sons and I have operated upon 900 in the last eight years.
Arnold S. Jackson, Madison, Wis.	Possible	Possible	I have seen one questionable case.	1,200 appendectomies have been done in the Jackson Clinic.

TABLE I—CONT'D

SURGEONS	DO YOU BELIEVE THAT TRAUMATIC APPENDICITIS IS A DEFINITE ENTITY?	CAN APPENDICITIS BE PRODUCED BY A STRAIN?	HAVE YOU EVER SEEN A CASE CAUSED BY TRAUMA?	NUMBER OF CASES OPERATED IN THE PAST TEN YEARS
Thomas M. Joyce, Portland, Ore.	Yes	I am not sure it could be caused by a strain.	One case caused by a direct blow.	My associates and I have operated upon 1,900.
Frank H. Lahey, Boston, Mass.	No	No	No	Did not state
O. F. Lamson, Seattle, Wash.	Only by a direct blow over the region of the appendix.	No	One. A direct blow on the abdomen and the patient developed acute appendicitis within two or three days.	About 300
E. Martin Larson, Great Falls, Mont.	I do.	No	No	600 or 800
Edwin P. Lehman, University, Va.	I suppose it is pathologically possible that a direct contusion of the appendix might initiate appendicitis. In view of the frequency of the disease, I do not see how even a history of a blow on the abdomen could be proven as the cause of any case of appendicitis. In any event, it would be a rare occurrence.	No	No	Almost 1,500
LeRoy D. Long, Oklahoma City, Okla.	Only where there is direct trauma.	No	One. A horse stepped on a little boy's abdomen and there was a traumatic division of the appendix.	Approximately 500

J. M. Mason, Birmingham, Ala.	No	No	No	Several hundred
Michael L. Mason, Chicago, Ill.	No	No	No	About 250
Richard H. Miller, Boston, Mass.	No	No	No	Did not state
Charles F. Nassau, Philadelphia, Pa.	No	No	No	Did not state
John R. Nilsson, Omaha, Neb.	No	No	No	Several hundred
Alton Ochsner, New Orleans, La.	Trauma might cause an acute exacerbation in an appendix in which there is latent infection.	No	No	Approximately 2,000 to 3,000
Thomas G. Orr, Kansas City, Mo.	No	No	No	At least 600
Ashley W. Oughterson, New Haven, Conn.	Trauma may cause inflammation but rarely or almost never in the appendix.	No	No	100
Grover C. Penberthy, Detroit, Mich.	No, except where trauma may aggravate a gangrenous appendix or cause an appendical abscess to rupture.	No	No	Estimated 800
Edward W. Peterson, New York, N. Y.	No	Possible but hardly probable.	One, and that doubtful.	Did not state
Damon B. Pfeiffer, Philadelphia, Pa.	No	No	No	Roughly 4,000 to 5,000

TABLE I—CONT'D

SURGEONS	DO YOU BELIEVE THAT TRAUMATIC APPENDICITIS IS A DEFINITE ENTITY?	CAN APPENDICITIS BE PRODUCED BY A STRAIN?	HAVE YOU EVER SEEN A CASE CAUSED BY TRAUMA?	NUMBER OF CASES OPERATED IN THE PAST TEN YEARS
I. S. Ravdin, Philadelphia, Pa.	Not in the sense in which it is commonly used, but I have seen contusion of the appendix.	No	Yes, traumatic amputation.	Almost 2,000
J. Sumter Rhame, Charleston, S. C.	No	No	No	800 to 1,000
Mont R. Reid, Cincinnati, Ohio	On a few occasions it has appeared to me that trauma has initiated acute appendicitis.	Yes	Yes	2,000 by various members of the staff
Ralph T. Richards, Salt Lake City, Utah	No	No	No	2,013 by staff of Salt Lake Clinic
J. Stewart Rodman, Philadelphia, Pa.	I am not at all sure that there is such an entity as traumatic appendicitis.		It is my definite impression that I have seen over the years a very few cases following trauma in which that may have been a factor in the etiology. I am inclined to believe, however, it was coincidental rather than the actual cause.	Several hundred
Erwin R. Schmidt, Madison, Wis.	I believe it is possible.	No	One or two cases where it was difficult to say that it was not due to trauma.	1,303 by myself and associates since 1924
Carlo S. Scuderi, Chicago, Ill.	No	No	No	About 300

Lindon Seed, Chicago, Ill.	No	No	No	Approximately 350
Charles F. Sherwin, St. Louis, Mo.	Yes, rarely.	Rarely	No	Probably 60 to 70
Arthur M. Shipley, Baltimore, Md.	I do not believe a blow on the abdominal wall is a predisposing factor in the development of appendicitis.	No	No	627 from 1930 to 1937
Albert O. Singleton, Galveston, Tex.	No	No	No	About 600
Calvin M. Smyth, Jr., Philadelphia, Pa.	Only as an acute exacerbation of a previously damaged organ.	No	Yes, two cases in twenty-one years.	Approximately 1,200
Samuel A. Thompson, New York, N. Y.	Possible, but very unlikely as a sole condition.	No	No	300
Clarence G. Toland, Los Angeles, Calif.	No	No	No	400
Elmer D. Twyman, Kansas City, Mo.	Yes	No, not produced (unless pinched in a hernia, etc.) but precipitated; appendix not previously normal.	Yes, in harvest laborers, wrestlers and a few accidents.	About 1,200
Fremont C. Vale, Detroit, Mich.	Yes, but very rarely.	No	No	Approximately 2,500 including those done by my assistants.
Frederick T. Van Beuren, Jr., New York, N. Y.	I doubt it.	I cannot see how it could be.	No	Very few, retired from active work.
Arkell M. Vaughn, Chicago, Ill.	No	No	Possibly one.	Approximately 500

TABLE I—CONT'D

SURGEONS	DO YOU BELIEVE THAT TRAUMATIC APPENDICITIS IS A DEFINITE ENTITY?	CAN APPENDICITIS BE PRODUCED BY A STRAIN?	HAVE YOU EVER SEEN A CASE CAUSED BY TRAUMA?	NUMBER OF CASES OPERATED IN THE PAST TEN YEARS
Benjamin N. Wade, Portland, Ore.	Do not think so, although I have had one case that followed abdominal trauma.	No	No	678
Irving J. Walker, Boston, Mass.	No	No	No	Approximately 2,000
John B. Walker, New York, N. Y.	Doubtful	No	No	300
Owen H. Wangensteen, Minneapolis, Minn.	Trauma which severed appendical vessels or caused obstruction to appendical lumen might cause it.	No	No	More than 1,000 in the University Clinic, the majority operated upon by my associates.
J. Ogle Warfield, Jr., Washington, D. C.	No	No	No	Approximately 600
John M. Waugh, Mayo Clinic, Rochester, Minn.	Not convinced that it is a definite entity.	Hard for me to conceive of any sort of a strain causing appendicitis.	No	2,500 to 3,000 cases operated upon at the Mayo Clinic. In this series I am unaware of any patient with so-called traumatic appendicitis.
J. Calvin Weaver, Atlanta, Ga.	No	No	No	Probably 75 to 100
Samuel D. Weaver, Dallas, Tex.	Yes, but it is an extremely rare thing.	No	One. A young, thin-walled woman who was brutally kicked in the abdomen.	Approximately 800
Charles S. White, Washington, D. C.	No	No	No	1,500 to 2,000

Morehead has stated that it is highly improbable that any violence could produce a lesion of such a deep-seated, movable, well-protected, tiny piece of intestine, and yet do no damage to surrounding intestine near the source of violence and far more vulnerable. In answer to this, Ludington asserts that the deep location and the mobility of the appendix would, indeed, be safeguards against injury if the abdomen were a solid body and, in obedience to the laws of physics, transmitted a received force only in the direction in which the force was applied. But the abdomen is not a solid body; it is essentially a liquid and gaseous mass and is subject to the laws governing the transmission of force by liquids and gaseous mediums; i.e., the pressure exerted on it is transmitted equally in all directions. The deep location of the appendix, therefore, is not a factor that contributes either to the liability of the appendix to damage resulting from external violence, or to its immunity in such an accident.

If the contention of Ludington's that the force is transmitted equally in all directions is correct, then there would be as much pressure applied to the appendix as to the cecum, and the contents of the cecum could not be forced into the appendix.

As evidence that the contents can be forced into the appendix, numerous authors claim that, following a barium meal, the barium can be forced from the cecum into the appendix by light manual pressure. I asked the opinion of a number of roentgenologists regarding this procedure, and it was the consensus that rarely, if ever, could barium be forced into the appendix by manipulation of the cecum. F. B. Stephenson stated that he does not believe that he ever filled an appendix by manipulation of the cecum following a barium meal or barium enema. K. D. A. Allen said: "In fluoroscopy study of the colon, I find it very difficult indeed, to visualize the appendix by barium enema." L. D. Crosby said: "I have never been conscious of filling an appendix by manipulation following a barium meal, and I do not believe it possible; unless the opening into the lumen of the appendix is unusually large."

According to Spicer, increased intraintestinal pressure causes pressure hemorrhage at the antimesenteric surface of the intestine. McCarthy and Magrath claim that the blood supply to the appendix may be occluded by external trauma, causing appendicitis or gangrene. Wells, experimenting on rabbits, showed that ligation of the appendicular artery and vein did not produce any obvious change in the appendix. In like manner, ligation of the mesoappendix failed to produce any change in the appendix. However, ligation of the appendicular vessels and the mesoappendix was followed by gangrenous appendicitis and death occurred in three days.

In view of Wells' findings, it would seem to me that any injury severe enough to cause appendicitis, by interference with the blood

TABLE II*

HOSPITALS	ACUTE APPENDICITIS CASES OPERATED UPON	CASES GIVING HISTORY OF TRAUMA
Baptist Memorial, Memphis, Tenn.	4,868	None
Bellevue, New York, N. Y.	4,446	None
Cedars of Lebanon, Los Angeles, Calif.	1,026	One. Severe strain of abdominal and intercostal muscles.
City Hospital, Baltimore, Md.	1,037	None
Colorado General, Denver, Colo.	484	Two. Man aged 37 years, pitching horseshoes when suddenly seized with severe pain in the pit of his stomach. Pain subsided in a short time, but returned later and was followed by nausea and vomiting. At operation, an acute appendicitis was found, but no evidence of trauma. Second case was that of a man aged 27 years, who was pulling up turnips in a garden, when he developed a pain over the entire abdomen. The pain became more severe, and he was operated upon twelve hours later. At operation, an acute appendicitis was found, but no evidence of trauma.
Columbus, Seattle, Wash.	1,287	One
Corwin, Pueblo, Colo.	642	None
Fitzgerald-Mercy, Darby, Pa.	575	One
General, Fresno, Calif.	1,800	None
General, Kansas City, Mo.	1,084	None
Grace, Detroit, Mich.	4,270	One
Graduate, University of Pennsylvania, Philadelphia, Pa.	1,122	None
Indianapolis City, Indianapolis, Ind.	1,981	None
Johns Hopkins, Baltimore, Md.	1,000	One
Mercy, Pittsburgh, Pa.	3,963	None
New York, New York, N. Y.	1,960	None

*All cases were operated upon between 1929 and 1938 with the following exceptions: Cedars of Lebanon, 1930-1938; Fitzgerald-Mercy, 1933-1938; St. Lukes, San Francisco, 1934-1938; San Francisco Hospital, 1927-1937; University Hospital, San Francisco, 1928-1937.

TABLE II—CONT'D

HOSPITALS	ACUTE APPENDICITIS CASES OPERATED UPON	CASES GIVING HISTORY OF TRAUMA
Passavant, Chicago, Ill.	900	None
Peter Bent Brigham, Boston, Mass.	866	None
St. Luke's, Kansas City, Mo.	750	None
St. Vincent's, Portland, Ore.	1,222	None
San Bernardino Charity, San Bernardino, Calif.	1,709	Two. In one a pin was found in the appendix. The other was struck in the abdomen with a sling.
Temple University, Philadelphia, Pa.	Did not state	None
Union Memorial, Philadelphia, Pa.	1,970	None
University, Augusta, Ga.	1,357	None
University, Baltimore, Md.	2,418	None
University of Kansas, Kansas City, Kan.	More than 600	None
University of California, San Francisco, Calif.	468	One. Intussusception.
Western Pennsylvania, Pittsburgh, Pa.	2,624	One. A direct blow on the abdomen with hemorrhage.

supply of the appendix, would cause considerable damage to the cecum and surrounding intestine, as well as to the abdominal wall.

Robinson advances the theory that action of the psoas muscle may act as a mechanical factor in producing appendicitis in those cases in which the organ lies on the muscle. Powerful contractions of the muscle irritate the appendix, causing adhesions, bands, angulations, kinks, and obstruction. If such were the case, a large number of individuals with retrocecal appendices would have developed appendicitis in childhood following such exercise as bicycling.

Wangensteen said: "Whereas there may be other causes of appendicitis than obstruction, the only tangible cause is obstruction, and it would appear that this cause alone will suffice to account for all the varieties observed clinically. Fecaliths and swelling of lymphoid tissue are probably the most frequent causes of appendical obstruction in man."

If trauma plays any part in acute appendicitis, it is certainly rare. I cannot accept the theory that trauma forces cecal contents into the appendix or forces fecaliths farther into the appendical lumen. If this were a fact, then we should see a lot more cases of acute appendicitis following the large number of automobile accidents seen today. I can conceive of an appendix being traumatized by a direct blow,

if it lay over the brim of the pelvis; or it could possibly be bruised, if it were close to the anterior abdominal wall in an extremely thin individual, but I believe that in such instances there would be other evidence of trauma.

Kessler asserts that laborers, who exert a great deal of back and abdominal strain, manifest very little, if any, appendicitis. I think this contention will be corroborated by the majority of surgeons doing industrial work.

Fowler says that genuine traumatic pathology is rarely demonstrated in the appendix, when compared with the frequency with which contusion, hematoma, laceration and rupture or perforation are encountered in other abdominal organs.

As White states, it is a well-known fact that people are prone to establish a connection between any disability and an accident which may furnish a possible cause for it, and this is especially true if the question of compensation or liability enters into it.

Ludington and Fowler believe that the most important and reliable information bearing on the question of trauma as the causative factor of an appendicitis is obtained at operation. Rhodes said, "Whatever the mechanism of the production of appendicitis, the inflamed edematous viscus, covered with fibrin and filled with pus or perhaps gangrenous, will tell little of the story of its initiating pathology. Free blood in the peritoneal cavity or histological evidence of trauma are requisite findings."

Several authors, among whom are Fowler and Kessler, have enumerated features which they personally believed necessary to evaluate the part played by trauma in the etiology of appendicitis. Because of the importance of this subject from a medicolegal aspect, I should like to see the Council on Industrial Health of the American Medical Association establish some criteria which would guide us in determining whether or not trauma should be considered as an etiologic factor in a given case of appendicitis.

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FEVER THERAPY IN THE TREATMENT OF MECHANICAL INTESTINAL OBSTRUCTION DUE TO PELVIC INFLAMMATORY DISEASE

Report of Two Cases

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MECHANICAL intestinal obstruction due to pelvic inflammatory disease is not a frequent occurrence. Levine and Blinick,[1] in their study of the subject, found but few references in the literature pertaining to intestinal obstruction secondary to inflammatory disease in the pelvis. They reported 3 cases and mentioned 36 cases found in the literature; however, no distinction was made as to the etiology of the adnexitis. Two of their cases were of gonococcal origin and one was postabortal. Thaler[2] described 3 cases of apparently specific pelvic inflammatory disease complicated by mechanical intestinal obstruction; Kaufman[3] reported 1 case; Périn,[4] 1 case; Martens,[5] 1 case; and Holtz,[6] 1 case.

In 7 of the above 9 cases, the obstruction was caused by agglutination of one or more loops of intestine to the inflammatory mass; the remaining 2 obstructions were due to adhesive bands. Flesch-Thebesius[7] reported 15 cases of obstruction secondary to pelvic inflammatory disease, but he did not state the type. He believed that most of these obstructions were caused by the string type of adhesion but that multiple adhesions were the cause in several. Turunen[8] reported 12 cases of obstruction due to adnexitis and stated that many were postabortal; in only 2 cases was the bowel closely adherent to the inflammatory mass.

Turunen explains the low incidence of mechanical intestinal obstruction as a complication of pelvic inflammatory disease upon the fact that the sigmoid colon, lying in juxtaposition with the inflammatory process, becomes adherent and prevents contact with the small bowel. Diarrhea frequently results, but seldom does obstruction occur. Levine and Blinick state, as does Turunen, that intestinal obstruction is usually a complication of chronic or subsiding infection, yet in 10 of the 39 above-mentioned cases the process was acute. According to Levine and Blinick, the mechanism of obstruction is usually kinking of an intestinal loop by retraction of the pelvic mass attending evacuation or healing of this mass.

It had been noted by many clinicians that gonorrheal infections were benefited by intercurrent infection in which there was a rather marked elevation of body temperature for an appreciable period of time. The treatment of gonococcal pelvic inflammatory disease by means of hyper-

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thermia has been extensively developed since the work of Carpenter, Boak, Mussi, and Warren[9] on the thermal death time of cultured gonococci.

In 1932 Warren and Wilson[10] reported the treatment of 9 cases of pelvic masses associated with gonococcal infection by means of general artificial fever brought about by mechanical means. Since that time many writers have included cases of pelvic cellulitis in their reports of gonorrheal infections treated by hyperthermia. All have been highly successful. Simpson[11] stated that the combination of Elliott treatment with the fever therapy lessened the required number of treatments; and Krusen, Randall, and Stuhler[12] advised the simultaneous administration of general artificial fever and either pelvic diathermy or Elliott treatment, because higher pelvic temperatures were obtained and the percentage of remissions was greater.

Bierman and Horowitz[13] reported that, following systemic fever therapy combined with pelvic diathermy, pelvic masses due to gonococcal infection begin to decrease in size from the seventh to the tenth day after treatment; pain usually disappears during the treatment. About two weeks after the treatment, the masses become very much smaller. Five of their 18 cases showed some residual enlargement of the adnexa two months after fever therapy. However, the adnexa were much smaller, and the mobility of the uterus was much greater in these cases.

In a recent review[14] of the 190 cases of mechanical obstruction of the small intestine seen in this clinic during the past seven years, it was noted that fever therapy was administered to two patients whose obstructions were caused by gonorrheal pelvic inflammatory disease. These patients were both seen during the past year.

CASE REPORTS

CASE 1.—V. H. (663530), a married white female, aged 37 years, was referred to the outpatient department Nov. 8, 1937, with a diagnosis of "emaciation and abdominal pain following surgical treatment for intestinal obstruction, peritonitis, and left tubal abscess 11 weeks ago." The patient complained of severe, sharp pain in the abdomen and vomiting; neither had been present for several days before coming to the University Hospitals.

She gave a history of uterine polypectomy in 1930 and again in 1934. She had gonorrhea with pelvic infection in 1933; this was treated and said to be cured. She also had an appendectomy in 1933. There was an acute exacerbation of the pelvic inflammatory disease in 1936. This was again treated and said to be cured. She had had no pregnancies.

She had had no symptoms or complaints for six months when in August, 1937, she suddenly developed crampy, colicky abdominal pain associated with nausea, vomiting, and distention. She was operated upon in another hospital twenty-four hours later for intestinal obstruction. At this time, a left tubal abscess was removed. There was considerable abdominal distention postoperatively, and there was continuous drainage from the lower end of the low midline incision. The patient was discharged after forty days of hospitalization with the sinus still draining foul pus; she had constant diarrhea. She remained bloated and had several

short attacks of abdominal cramps associated with vomiting. The last of these had occurred several days before coming to this clinic.

Physical examination revealed a white woman of the stated age in a state of fair nutrition, weighing 126 pounds. No abnormal findings were present except in the abdomen and pelvis. There was a healed McBurney scar and a lower abdominal midline scar, from the lower end of which foul pus was draining. Introitus was nulliparous and would not admit two fingers. Examination of Bartholin's and Skene's glands was negative. There was moderate vaginitis and the cervix was nulliparous. The cervix pointed downward and backward. The uterus and adnexa were bound down and immovable. Cervical and urethral smears were negative for gonococci. Diagnosis was chronic pelvic inflammatory disease. She was given eight Elliott treatments and a course of sulfanilamide without appreciable improvement and was sent home for a rest period.

She returned Jan. 18, 1938, acutely ill, with a twenty-four-hour history of severe crampy abdominal pain, nausea, and vomiting. She had vomited six or seven times. The emesis was normal gastric contents. Examination revealed a well-developed and nourished white female of stated age, acutely ill, and moderately dehydrated; temperature, 99.6° F.; pulse, 96; respiration, 20; and blood pressure, 140 mm. systolic and 100 mm. diastolic. Examination of the head, neck, chest, and extremities was essentially negative. The abdomen was 2+ distended and a suggestion of visible peristalsis was present. The sinus at the lower end of the old midline scar was draining foul pus. There was generalized abdominal tenderness, maximum in the right lower quadrant where rebound tenderness was present; no masses were palpable. Borborygmi were heard at the acme of pain. The pelvic viscera were fixed by cellulitis. Hemoglobin was 72 per cent; white blood cells, 10,400 per c.mm. of blood; 76 per cent of these cells were polymorphonuclears, and 24 per cent were lymphocytes. The urine was negative. Blood nonprotein nitrogen was 38.7 mg. per cent, chlorides were 596 mg. per cent, and the carbon dioxide combining power was 56 volumes per cent. Scout films of the abdomen showed small bowel obstruction with very marked gaseous distention of some small bowel loops.

Diagnosis was mechanical obstruction of the small intestine, but colonic obstruction could not definitely be excluded so exploration was done the evening of admission. The abdomen was opened through a midleft rectus incision; no free fluid was present. The small intestine was dilated and had an abnormally thick wall. The omentum was adherent to the contents of the pelvis, and no further exploration was deemed advisable. Wangensteen's modification[15] of the Witzel type of enterostomy was done and intraluminal pressure, as determined through the enterostomy catheter, was 14 to 18 cm. of water, varying with respiration.

Surgery was well tolerated. Duodenal suction was instituted preoperatively and was continued for five days after operation. Suction was applied to the enterostomy catheter; drainage was profuse for the first week but diminished thereafter. Clamping of the enterostomy catheter was tolerated, and it was removed on the fifteenth day after operation. Cervical and urethral cultures were negative for gonococci Feb. 1, 1938, and cultures taken from the old midline sinus Feb. 2, 1938, were sterile. The patient tolerated a soft diet satisfactorily until the twenty-second postoperative day when abdominal cramps and vomiting recurred. Duodenal suction was again instituted, and a radiogram the next day showed markedly distended loops of small intestine. Suction was discontinued after seven days but was started the following day because of cramps, vomiting, and distention. Elliott treatments and hot sitz baths were begun at this point. During the next ten days suction was discontinued for only two days. The patient had been given transfusions and intravenous fluids during the periods of suction. Blood chlorides and serum proteins were normal, and the patient's weight was 120 pounds. The sinus had closed.

Fever therapy was advised by Dr. O. H. Wangensteen and on Feb. 25, 1938, the thirty-ninth postoperative day, this was begun, using the Kettering hypertherm under the direction of Dr. M. M. Cook. The patient was submitted to a temperature of 100.5 to 101° F. rectally for two hours on Feb. 25, 1938. She tolerated this well. Suction was removed Feb. 27 and was not used again. On March 1, her temperature was maintained at 101.5 to 102° F. rectally for three hours. Other treatments were as follows: March 4, 103.5° F. for three hours; March 9, 103.5 to 105° F. for three and one-half hours; and March 14, 103 to 104° F. for three hours. Her weight on March 14 was 120 pounds. She was discharged March 18, 1938, the sixtieth hospital day, eating a low residue, high caloric diet and taking mineral oil daily. She was instructed to take daily hot douches.

The patient was seen April 20, 1938, and stated that she had been well except that she had had a bout of abdominal cramps the second day after discharge; these cramps lasted five to six hours and were relieved by bed rest and a hypodermic injection. The corpus uteri was in second degree retroversion and the adnexa were relatively free from induration. She was again seen Dec. 30, 1938; about ten days before this she had had a short bout of cramps similar to the attack shortly after discharge. Menstrual periods had been regular every three weeks for the first three months following discharge and had then become regular every four weeks. She noted bloating before each period and her last period had started four days after her recent abdominal cramps. For the last month she had been eating a high residue type of diet, not advised by a physician, to do away with bloating. Her weight was 165 pounds.

Physical examination was negative except for the abdomen and pelvis. There was herniation of the lower midline incision with bowel visible and palpable immediately below the skin. Introitus was nulliparous; the urethra was clean; Bartholin's and Skene's glands were negative; and the cervix was clean although there was a small transverse laceration of the os. The corpus uteri was normal in size and shape and was freely movable. The left adnexa was negative; on the right there was a slightly tender, irregular induration extending from the right cornu of the uterus to the right side of the cul-de-sac. Here the right ovary was palpable and slightly enlarged. Cervical and urethral spreads and cultures were negative for gonococci. Because of the incisional hernia and the history of low-grade, intermittent obstruction, hernioplasty and concomitant enterolysis were advised.

The patient was admitted Jan. 16, 1939, with findings as above with the exception that at this time a mass was palpable in the left adnexa. A long double lumen tube with a terminal balloon was passed to the region of the terminal ileum in the pelvis; beyond this it would not progress. The balloon was deflated and barium sulfate mixture was injected. The ileum at this point, approximately one and one-half feet from the ileocecal valve, was fixed in the pelvis, and the mucosa was tented out in two areas with a concavity about one inch in length between the two "tents." There was stasis in this region; there was also some stasis in the region of the midileum.

At operation, Jan. 19, 1939, the lower one-half of the small bowel was thickened, and the lumen was larger than normal; this was most marked in the region of the terminal ileum. Here the collapsed bowel measured approximately 5 cm. from mesenteric to antimesenteric border. There were a number of stringlike adhesions between the various loops, but the patient's principal difficulty lay in very dense adhesions in the cul-de-sac where a loop of ileum was adherent to the posterior surface of the uterus and to the posterior pelvic wall. Beyond this, the ileum appeared normal. The right tube was dilated and bound down in the cul-de-sac. The sigmoid was also attached behind the uterus. The right ovary was cystic, and the cysts were punctured. An enterolysis and salpingectomy were done. The denuded area of ileum was sutured over, and omentum was brought down

into the pelvis. The hernia was repaired. Microscopic examination of the right tube revealed chronic salpingitis with hydrosalpinx.

Convalescence was uneventful, and the patient was discharged Feb. 3, 1939, the sixteenth postoperative day. She was seen a month later and had had no symptoms of obstruction. She stated in June, 1939, that she felt bloated for two or three days two weeks before each menstrual period; however, she had no cramps, nausea, or constipation.

CASE 2.—G. C. (667531), a married white female, aged 24 years, was admitted to the gynecology service March 25, 1938. She complained of abdominal pain and irregular menses. On Jan. 10, 1938, she began a regular, normal five-day period; during February no menses appeared and the patient believed she was pregnant. However, March 6, 1938, menstrual flow began and continued, with clots present, intermittently for ten days. With the irregular flow, the patient had right lower quadrant pain and occasionally a sharp right shoulder strap pain which the patient attributed to pleurisy. Bleeding stopped, and the patient was free from pain for about one week. Pain and intermittent bleeding recurred March 21, 1938, and the pain became severe March 23. Pain on defecation and urination was present.

Past history revealed that the patient had had an appendectomy for chronic appendicitis three years before and had had a salpingectomy for left tubal pregnancy two and one-half years before. She had been married twice; in February, 1938, primary syphilis was found in the patient and her husband and treatment was begun.

Physical examination revealed a chronically ill, thin woman who appeared somewhat older than her age. Temperature was 99.2° F.; pulse, 104; respirations, 20. Pupils were normal. There were no mucous membrane lesions, and no skin lesions of note. There was slight distention of the abdomen and healed right lower quadrant and midline suprapubic scars were present. There was tenderness and rebound tenderness over the lower abdomen, more marked on the left. Introitus was marital and mucopurulent discharge was present. There was a minimal cervical erosion; the corpus uteri was anterior and normal in size. Motion of the uterus was painful. There was a mass 4 by 4 by 6 cm. in the right adnexa with thickening and marked tenderness in the right adnexa; the left adnexa was similar, but the mass present on the left was smaller. Laboratory data of note were hemoglobin of 72 per cent, 13,400 leucocytes per c.mm. of blood, 93 per cent of which were neutrophiles. Urinalysis was normal except that numerous white blood cells were present. Cervical and urethral smears were negative for gonococci. Blood Wassermann was four plus positive. Diagnosis was acute exacerbation of chronic pelvic inflammatory disease with pelvic peritonitis, ectopic gestation to be excluded, and syphilis.

Treatment consisted of duodenal suction, parenteral fluids, hot packs to the abdomen, and sedation. However, the patient continued to have pain; and March 29, 1938, her temperature was 101.2° F. rectally and her abdomen was moderately distended. The pelvic induration was less, but the masses were the same. Scout films of the abdomen showed numerous dilated small bowel loops with little gas in the colon. The films were interpreted as mechanical small bowel obstruction by the roentgenologist. White blood count was 5,000 cells per c.mm. A cul-de-sac puncture was done, and 35 c.c. of sterile straw-colored fluid were removed. Rapid improvement began, and the patient was discharged April 6, afebrile, free from pain, and eating a full diet.

She was seen one week later in the outpatient department; she stated that she had had considerable pelvic pain with some nausea and vomiting but felt better. Pelvic examination was essentially unchanged.

On April 21, 1938, the patient had recurrence of abdominal pain, distention, and vomiting and was admitted to another hospital and transferred to the Uni-

versity Hospitals April 23 where she was again admitted to the gynecologic service. She stated that she had had gas pains and fecal vomiting. Temperature was 99.6° F. by mouth and the pulse was 100. The patient was dehydrated. The skin of the abdomen was pigmented from application of heat and the scars were again noted. There was moderate gaseous distention and moderate tenderness, but no rigidity. The abdomen was reported as silent. The hemoglobin was 87 per cent; there were 13,600 leucocytes per c.mm. of blood. Urinalysis was negative. Radiograph of the abdomen revealed marked gaseous distention of several loops of small bowel with gas present in the stomach and ascending colon. Diagnosis was subsiding pelvic inflammatory disease, low-grade intestinal obstruction, and syphilis. A note made later on the evening of admission reported the patient to be doubling up with cramps from time to time.

Conservative treatment was instituted, and the patient improved so that suction was discontinued April 28. An enema given that day was expelled with much flatus. The patient felt fine until May 3 when crampy pain, distention, and vomiting recurred. The abdomen was moderately distended, diffusely tender, and tympanitic. There was a questionable doughy mass in the right lower quadrant. Conservative treatment was again begun. The patient was seen by the surgical staff May 4, and a diagnosis of mechanical small bowel obstruction secondary to pelvic inflammatory disease was made. Scout films showed marked distention of the small bowel. Decompression was effected by means of a long double lumen tube. However, the patient could not tolerate clamping of the tube, and, after numerous attempts, fever therapy was begun on May 18.

The twenty-sixth hospital day, May 18, the first fever treatment, consisting of a temperature of 103 to 104.5° F. rectally for two hours, was given. This treatment was well tolerated. The patient's weight at that time was 84 pounds. Suction was discontinued May 20 after clamping of the catheter had been tolerated. The patient had occasional nausea and small emeses until June 4; however, neither cramps nor distention appeared. Other treatments were: May 23, 1938, 104° F. for three hours; May 26, 104° F. for three hours; June 1, 103° F. for three hours; June 7, 104° F. for three hours; and June 10, 104° F. for three hours. During the course of fever therapy, the patient's weight had dropped to 70 pounds, but it had risen to 78 pounds at the conclusion of treatment.

She was discharged June 14, 1938, ambulatory and feeling well. Examination of the pelvis revealed the corpus to be normal in shape, fairly movable, and in first degree retroversion; the right ovary was prolapsed and was moderately adherent to the lateral surface of the corpus; there was some thickening of the left adnexa. The gynecologic opinion was that there had been marked resolution of the pelvic inflammatory disease.

The patient was instructed to eat a low residue diet and take mineral oil, and when seen in the outpatient department Aug. 26, 1938, she was free of symptoms. In a follow-up letter received in December, 1938, she stated she had had a few slight abdominal pains and occasional lower abdominal ache, but had not been confined to bed; she had had no leucorrhea.

DISCUSSION

The hyperpyrexia regime of necessity must be particularly carefully supervised in these patients. The patient is weighed immediately before and the day after each treatment. Therapy is delayed until a positive or stationary weight balance is maintained if possible. If the patient is unable to stand, she is weighed upon a litter. An enema, if necessary, and sedation are given the evening before therapy. Breakfast

is omitted, and, if suction is being employed, paraoral fluids are given. Morphine in appropriate dosage is used for sedation; no morphine is used between treatments unless absolutely necessary. Fluids, administered intravenously or subcutaneously, are given at the termination of fever.

The importance of dehydration, chloride depletion, and alkalosis in artificial fever has been pointed out by Warren[16] and others. In the presence of intestinal obstruction, these factors are more readily thrown out of balance. The chloride content of the blood is checked frequently and any deficiency is corrected by the parenteral administration of physiologic saline solution. The carbon dioxide combining power of the blood is determined upon admission and subsequently as indicated. If the chloride content is normal, there should not be alkalosis. The state of hydration is followed by observation of the urine output (a urine output of 600 to 1,000 c.c. per twenty-four hours being maintained by liberal paraoral administration of fluid) and by determination of the specific gravity of the blood serum. While suction is being employed or the diet is restricted, the plasma proteins are determined from time to time, and, if they are low, transfusions are given. A "wet" chamber is used to produce and maintain fever; Gibson, Kopp, and Evans[17] showed fluid and chloride losses by perspiration are less and hyperventilation is less marked than when a "dry" chamber is used.

In all likelihood, with the resolution of the inflammation, mobility of the adherent intestinal loops is increased, edema is decreased, and intestinal obstruction due to traction and kinking is relieved. The string type of adhesion is probably affected but little, but since "strings" are rather long, decompression should allow release of the obstructing mechanism in most cases. From reported cases one obtains the impression that most mechanical intestinal obstruction in gonorrheal adnexitis is caused by agglutination of intestinal loops to the inflammatory mass; it is probable that this is true in most of the cases resistant to the usual conservative regime.

Hench, Slocumb, and Popp[18] state that the presumable clinical benefits of fever therapy are due to: (1) bacteriolytic or bacteriostatic action of heat; (2) increase in formation or mobilization of immune bodies; (3) local effect from vasodilation; and (4) general effect of heightened metabolism. While it has been generally considered that fever therapy is remarkably successful in gonorrhea because the gonococcus is killed by fever which is tolerated by man, prior to the work of Studdiford, Casper, and Seadron[19] the gonococcus was infrequently found in chronically inflamed adnexa. These authors obtained positive tubal cultures in 66 per cent of subacute and chronic cases and believe that organisms may remain for many years. One patient, whose tubal culture was positive, had salpingitis of at least ten years' duration, and another had had two eight-hour periods of artificial fever at 107° F.

Artificial fever has been used with variable success in a great many conditions where no specific action is present. It is quite possible that it would be of great aid in subacute pelvic peritonitis following appendical perforation. Diathermy has been employed here in one such instance, resulting in rapid localization and softening of the inflammatory process. The work being done upon the specific bacteriologic effects of ultrashort (Hertzian) waves in the future may open a new avenue of attack upon this problem.

SUMMARY

1. Two cases of mechanical small bowel obstruction, secondary to gonorrheal adnexitis, treated by hyperthermia are reported.

2. It is suggested that artificial fever may be of benefit in subacute pelvic peritonitis of nonspecific etiology.

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ANORECTAL COMPLICATIONS OF CHRONIC ULCERATIVE COLITIS, WITH SEVERAL ILLUSTRATIVE CASES

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ANORECTAL complications which accompany or follow chronic ulcerative colitis or thromboulcerative colitis are not infrequent, and the treatment of such complications requires the exercise of sound judgment if the accomplishment of more harm than good is to be prevented. Such complications, although in their basic features they resemble similar lesions which afflict otherwise healthy individuals, must be more carefully studied than usual; their relationship to the patient's immediate welfare and the possible result of surgical intervention must be considered seriously before any radical measures are instituted.

ANORECTAL ABSCESS AND FISTULA

The vulnerability of the crypts of Morgagni to infection is so well known that the occurrence of such complications as the ones to be described is not difficult to understand. In the study of 871 consecutive cases of chronic ulcerative colitis in which the patients were observed at the Mayo Clinic, it was learned that 73 patients, or 8.4 per cent of the entire group, had suffered development of anorectal abscesses or anorectal abscesses with subsequent fistulas. The frequency with which these lesions occurred was slightly greater among males (491 male patients, of whom 43, or 8.8 per cent, had an abscess or fistula) than it was among the females (380 female patients, of whom 30, or 7.9 per cent, had an abscess or fistula). Of 95 children under the age of 16 years in this group of 871 patients, 6, or 6.3 per cent, had suffered development of an abscess or fistula. This complication was found to rank third in order of frequency of occurrence, polyposis and stricture occurring more frequently in the order named. It is of interest, also, to observe that of the 3 patients whose condition terminated in death, there could be but little doubt that the formation of an acute anorectal abscess was the chief contributing factor in causing each fatality.

The anorectal abscesses and fistulas which complicate chronic ulcerative colitis manifest several peculiarities which are worthy of serious consideration and which probably explain, partially at least, several of the reasons these lesions deserve special study. Unlike the more common abscesses and fistulas occurring in the anorectal region of the body, these particular lesions do not seem to stimulate the formation of the usual firm, fibrous wall surrounding the abscess or fistula. Such a protective

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reaction appears to be minimal as it affects those patients whose chronic ulcerative colitis is most severe, and inversely, the reaction frequently is more marked among those patients whose colitis is mild. The primary or internal opening occurs as usual in the crypts of Morgagni, but it is often 0.5 to 1 cm. in diameter and the mucosal margin of such an opening, instead of being attached to the underlying tissues by scarring which results from the inflammatory process, appears as a loose, freely movable, irregular margin.

The destruction of tissue caused by the formation of the abscess often is extreme; especially is this true of the destruction of subcutaneous fat in those abscesses which invade portions beyond the perianal tissues. The abscesses occurring in the presence of chronic ulcerative colitis tend to vary from the more common type in their manner of progress; they will involve, frequently, several of the potential perianal spaces and almost as frequently progress simultaneously proximally and distally from the primary opening.

The incontinence of these patients is the frequent, ultimate result of tardily begun or inadequately completed natural protective measures, such as fibrosis and scarring. This result, while wholly undesirable, is often unavoidable because of the destruction of the involved portion of the external anal sphincter muscle or marked deformity of the anus, or a combination of both.

A patient afflicted with chronic ulcerative colitis and also suffering from anal incontinence is often relegated to the life of an invalid. It would seem, therefore, that if conservative measures can circumvent such a disaster they are extenuatingly justifiable. To the patient who has chronic ulcerative colitis, the presence of a fistula is a small price to pay if anal continence is thus insured.

ANAL INCONTINENCE

Anal incontinence afflicted 12 patients (1.4 per cent of the entire group), all of whom had been submitted to fistulectomies elsewhere. Some degree of anal incompetence is not uncommon among patients who become debilitated because of chronic ulcerative colitis. Undoubtedly, however, most patients would tolerate the inconvenience and discomfort of a fistula rather than sacrifice anal control as the price for the cure of the fistula.

The following abstracted reports of cases are presented to emphasize several of the unusual features of this disease: (1) the risk attendant upon any surgical manipulation; and (2) the unusual response of the involved tissues, causing remarkably prolonged convalescence and healing.

REPORT OF CASES

CASE 1.—A man, 26 years old, came to the Mayo Clinic in November, 1934, because of recurring episodes of bloody diarrhea, loss in weight, and abdominal cramps that had persisted for two years. Aside from the fact that he was emaciated and pale, the only significant observations were those referable to the large intestine.

Proctoscopic examination demonstrated chronic ulcerative colitis of activity 2 on the basis of 1 to 4. The lumen of the bowel was contracted about one-fourth. Roentgenologic studies of the colon disclosed that the entire colon was involved, with considerable narrowing and deformity.

On the ninth day after admission to the hospital, his temperature, which had varied from 98.6 to 99.8° F. (37 to 37.6° C.), increased to 103° F. (39.4° C.). At about the same time he complained of discomfort in the region of the right ischioanal fossa. The following day this region became tender, reddened, swollen, and indurated. Hot, moist packs were applied locally and general measures were instituted to relieve the pain.

On the sixth day following development of the abscess, definite fluctuation was noted. The external wall of the abscess was incised without anesthesia, and a stab wound was made into the cavity of the abscess. Several ounces of pus exuded. In spite of the fact that no attempt was made to enlarge the incision and the fact that it was felt that trauma had been limited to a minimum in providing drainage, the temperature of the patient increased promptly to 106° F. (41.1° C.) and evidence of severe toxemia persisted for the ensuing twenty-four hours, at which time the temperature returned to normal. Because of this patient's untoward reaction to a minimal surgical procedure, no attempt was made to repair the fistula.

CASE 2.—A woman, 28 years old, registered at the Mayo Clinic on March 17, 1938, because of an unhealed surgical wound that had followed an operation performed nine months previously for a fistula. For three years prior to coming to the Clinic she had had episodes of bloody diarrhea, with from six to fourteen passages of stools daily. Shortly after the onset of diarrhea, an abscess had developed on the left side of the anus; it had ruptured spontaneously and had continued to drain until the time of the fistulectomy.

On proctoscopic examination, the mucous membrane of the rectum appeared to be glazed, granular, and bled readily under trauma. Activity of the disease was graded 1 on the basis of 1 to 4. Posterior to, and extending into, the anal canal was a large, unhealed wound (4 cm. by 8 cm. in extent); the margins of this wound were smooth and its base was covered with abnormally excessive granulation tissue. In spite of the fact that nine months had elapsed from the time of the fistulectomy until the time she was seen at the Clinic, the wound showed little evidence of healing, even though the fistula apparently had been dealt with adequately. The discomfort caused by this wound had added immeasurably to the patient's disability.

STRICTURE

In the presence of chronic ulcerative colitis, the diameter of the anus appears to be altered differently among various patients. It will be discovered that the anus of some patients, when they are placed in the inverted position for sigmoidoscopic examination, appears to be patulous and of greater diameter than is normal. More frequently, however, anal contracture and actual formation of anorectal stricture will be disclosed by digital examination of the anus. The latter alteration is the result of one or more factors, such as irritation in the presence of infection, lack of the dilatation which is accomplished during the evacuation of a normal stool, and invasion of the anal and perianal tissues by infective bacteria, either of these tissues alone or in tissues contiguous to a similar invasion of the adjacent rectal wall.

The two factors mentioned first may cause a condition which, conservatively, might be called merely "anal contracture," but actual invasion

of the anal and perianal tissues by infective bacteria usually produces a real anal or anorectal stricture.

In the presence of chronic ulcerative colitis, stricture may occur in any portion of the rectum, sigmoid, or colon which is involved by the disease. Considering this fact and considering also the vulnerability of the dentate margin to injury and infection, it is surprising that anorectal strictures are not observed more frequently as accompaniments of this disease.

Anorectal stricture was observed 78 times (9 per cent) in the series of 871 cases studied. Anorectal stricture afflicted 43 (8.8 per cent) of 491 male patients and 36 (9.4 per cent) of 380 female patients.

As afflicting most of the patients, the stricture involved not only the anus but also the adjacent portion of the rectum. None of the patients observed required surgical treatment either locally or proximally, such as ileostomy, because of obstruction or other symptoms or effects.

ANAL ULCER

Twenty-seven (3.1 per cent) of the patients studied in this group had anal ulcers. This incidence is not great, but it does provide a problem of sufficient magnitude to justify special consideration. These ulcers are usually painful, cause pronounced anal spasm, and are not infrequently the site from which the constant secretion of serum and pus adds to the patient's discomfort, because of the cutaneous irritation thus initiated and aggravated. Some patients so afflicted will complain also of incontinence, which results from the gross deformity of the anus or from the patient's fear of contracting the sphincter sufficiently because of the pain such action would cause.

The ulcers vary considerably in size, conformation, location, and gross appearance. They may be solitary or multiple, isolated or confluent. Usually, their margins are rather ragged in appearance and overhang the base of the ulcer. The base of the ulcer frequently displays little evidence of normal healing processes; the ulcer appears to be irregular, not infrequently covered with a pseudomembrane, bleeds upon the slightest provocation, and on palpation little firmness, owing to fibrosis or scarring, can be detected. Granulation tissue, if present, may be excessive and also abnormally friable.

In such cases, it is advisable to treat anal ulcers palliatively, avoiding all surgical measures as much as possible. Cleansing of the part with warm solutions, such as witch hazel (Hamamelis), and applying non-irritating antiseptics, such as an aqueous solution of metaphen, usually will assist materially.

In addition to these measures, application of hot, wet packs to the anus and also one of the medicaments which in an ointment or water-soluble jelly will produce surface anesthesia, usually will alleviate some of the patient's discomfort. As a rule, however, such agents cannot be applied

with sufficient frequency to insure the patient's constant comfort. The amount of infection present and the patient's lowered resistance to infection would seem to preclude the injection of any anesthestic-bearing oily solution into the perianal tissues to overcome pain.

Oddly, when such ulcers as these have healed, the anus may contain, in addition to the deformity, strips of skin bridging the depressed scars, patently the result of the ulceration. These bridges of skin apparently result from the remnants of skin lining the anal canal under which the ulcers have burrowed. The subsequent healing of the base of such an ulcer as evidenced by the formation of granulation tissue and epithelization usually will cause the bridging remnant of skin to assume marked prominence, resulting in the unusual appearance mentioned.

ANAL FISSURE

Typical posterior or anterior anal fissures occurred among 24 patients (2.8 per cent) in the group of 871 studied. Fissures such as these are especially painful during the acute phase of chronic ulcerative colitis because of the trauma produced by the forceful expulsion of undigested food particles at defecation, but during the less active phase, when the stools are soft in consistency rather than liquid and are fewer in number, these fissures may cause little discomfort.

Surgical intervention performed in the attempt to eradicate the fissure seems inadvisable, especially when the primary disease is active. The topical application of such anesthesia-producing chemicals as metycaine, ethyl aminobenzoate, and similar agents and the application of heat locally by means of hot, wet packs usually will overcome severe discomfort. If surgical intervention is unavoidable, only minimal procedures should be attempted.

Superficial abrasions also frequently occur in the presence of chronic ulcerative colitis, and they deserve more serious consideration than do those observed in patients who are normal otherwise. Measures undertaken to insure local cleanliness, such as gentle bathing of the part with mild soap and water after each evacuation, assist materially in the prompt healing of such lesions as these.

HEMORRHOIDS

Hemorrhoids cannot be considered as complications of chronic ulcerative colitis in the same sense as the other lesions previously mentioned. Their presence, however, may add appreciably to the discomfort of the patient and may also increase the susceptibility of the anorectal tissues to infection. In our study of 871 cases, hemorrhoidal tissue was observed about as frequently as it would be in examining patients not afflicted with organic disease of the colon.

Thirty-two patients (3.7 per cent of the entire group of 871) stated that the symptoms of chronic ulcerative colitis were first noticed after

hemorrhoidectomies done elsewhere. Nearly all these patients consulted their physicians because of rectal bleeding. Following hemorrhoidectomy, not only did the symptoms of the colonic disease become more pronounced, but the resulting wounds healed very slowly.

Twenty-one patients, in addition to the 32 previously mentioned, had had a hemorrhoidectomy performed elsewhere after the symptoms of chronic ulcerative colitis had been observed for one or more years. Study of the cases represented by these patients emphasizes the need of sigmoidoscopic examination prior to the initiation of any rectal surgical treatment; such examination also will indicate the advisability of avoiding optional surgical procedures in the presence of chronic ulcerative colitis. The following abstracted history has been chosen because it illustrates the facts mentioned.

CASE 3.—In March, 1938, a man, 54 years old, registered at the Mayo Clinic because of uncontrollable diarrhea and bloody discharges of three years' duration. Two and one-half years prior to coming to the Clinic, he had consulted his physician because for a period of six months he had noticed the passage of blood after bowel movements. During that period he was having one formed stool a day. Hemorrhoidectomy was performed, the operation requiring him to remain in the hospital for three weeks. It required three months for the incision to heal. He continued to pass blood after healing was complete and began to pass from two to five stools daily, with blood. This condition had remained about the same until he was encountered at the Mayo Clinic. Proctoscopic examination demonstrated a scarred, contracted anal canal, above which the mucosa was slightly granular; it bled readily under slight trauma. The disease was active, 1 on the basis of 1 to 4. There was no contraction of the lumen of the bowel. Retrograde filling of the colon with opaque substance disclosed involvement of the left half of the colon.

SUMMARY AND CONCLUSIONS

1. Anal abscess or fistula is one of the most common complications of chronic ulcerative colitis. It afflicted 73 of 871 (8.4 per cent) consecutive patients whose records were studied. This condition ranked third among the complications, polyposis and stricture occurring more frequently, in the order named.

2. Indications for surgical interference in the treatment of anal conditions complicating or coexisting with chronic ulcerative colitis should be limited to emergencies, such as the formation of abscess.

3. Incision and drainage of abscesses should be carried out with a minimum of trauma.

4. The importance of careful proctoscopic examination is emphasized. Thirty-two patients (3.7 per cent) had a hemorrhoidectomy during the insidious initial stages of chronic ulcerative colitis. An additional 21 patients had an operation for hemorrhoids during the active course of the disease.

5. Stricture in the anorectal region occurred among 78 patients (9 per cent). For none of the patients was it necessary to do surgical intervention.

THE VASOCONSTRICTOR ACTION OF EPINEPHRINE ON THE DIGITAL ARTERIOLES OF MAN BEFORE AND AFTER SYMPATHECTOMY

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THE Meltzers'[28, 29] studies in 1903, the work of Elliott[11] in 1905, and subsequent investigations have shown conclusively that interruption of sympathetic nerves supplying smooth muscles of animals increases the contraction effect of epinephrine on the smooth muscles which have been denervated.[2, 3, 5, 7-12, 16, 18, 20, 26-29, 34, 40-43] Explanations of this physiologic phenomenon are theoretical and not pertinent to this presentation.[4, 8, 10, 31] Experimental studies on animals indicate that section of sympathetic nerve fibers distal to the sympathetic ganglia (postganglionic section) increases the contraction effect of epinephrine on smooth muscle more than section of sympathetic fibers proximal to the sympathetic ganglia (preganglionic section) does, although both procedures increase the sensitivity of smooth muscle to epinephrine.[3, 11, 16, 42] Ascroft's studies on the monkey indicated that postganglionic section increased the sensitivity of the smooth muscle of peripheral blood vessels to epinephrine about ten times; whereas, preganglionic section increased it only about three times.

It has been common observation that operation (lumbar ganglionectomy which is essentially preganglionic sympathectomy) for Raynaud's disease of the lower extremities uniformly results in cure; whereas, operation (cervicothoracic ganglionectomy, which is essentially postganglionic sympathectomy) for Raynaud's disease of the upper extremities produces less satisfactory results. Freeman, Smithwick, and White, by using a decrease in the temperature of the skin of the digits of man as a manifestation of sensitivity of arteriolar smooth muscle,[29] concluded that postganglionic denervation increased the sensitivity of the arterioles to epinephrine injected intravenously or liberated in the blood from the suprarenal glands as a result of hypoglycemia induced by injecting insulin.[15] Preganglionic section of sympathetic nerves seemed to increase the constrictor response of smooth muscle to epinephrine considerably less than did ganglionectomy.[6] Daniélopolu and his associates[9] had investigated this problem previously, by using the plethysmograph, and had found that after

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left cervicothoracic ganglionectomy (postganglionic section) for epilepsy intravenous injection of epinephrine caused vasoconstriction of a greater degree in the skin of the left fingers than in the skin of the right fingers. Six years later[10] they reported that unilateral lumbar ganglionectomy (preganglionic section) performed on animals and on man caused intravenously injected epinephrine to provoke greater vasoconstriction in the denervated extremities than in the normally innervated extremities. In 1936, Smithwick[36] suggested an operation much the same as that described the year previously by Telford,[38] by means of which preganglionic sympathectomy of the upper extremities was performed, thus simulating, anatomically, sympathectomy for the lower extremities. Smithwick's operation was devised to prevent the greatly increased sensitivity of digital arterioles to epinephrine which he believed was a major cause for failures following ganglionectomy (postganglionic section) for Raynaud's disease of the hands.[1] His reports indicated that the results have supported his logic. The operation described by him has in his opinion prevented, for the most part, the failures which frequently followed ganglionectomy for Raynaud's disease of the hands.

In a previous report, two of us (Fatherree and Allen) stressed the shortcomings of the method of determining sensitivity of smooth muscle to intravenous injection of epinephrine by determining decreases in temperature of the skin. It was observed that there were marked differences in the response of the skin temperature of the different digits of the same extremities on different occasions and in the response of the temperature of the skin of the same digits on different occasions as a result of injecting a dilute solution of epinephrine into the blood of patients with normally innervated extremities. This observation tended to indicate that the method of study was unreliable because of marked differences in responses under apparently identical circumstances. However, subsequent studies indicated that the differences mentioned are much less after sympathectomy than they are before; therefore, the method of study seems more reliable when denervated extremities are being investigated than when normally innervated extremities are studied. Nevertheless, if reliable conclusions are to be made by this means of study, the results should be definite and consistent. Two of us (Fatherree and Allen) found also that the digital arterioles of patients with Raynaud's disease were not necessarily more sensitive to epinephrine than were the digital arterioles of patients who did not have Raynaud's disease. It was found that some patients with marked decreases in skin temperature following intravenous injection of epinephrine, which indicated marked sensitivity of arteriolar smooth muscle, did not have Raynaud's disease. We felt that our observations cast considerable doubt on the conclusions of other investigators that failure of ganglionectomy to

relieve Raynaud's disease of the hands was due to increased sensitivity of digital arterioles to epinephrine, which was induced by ganglionectomy.

The present report, which is concerned with a continuation of the study previously reported by two of us (Fatherree and Allen), deals with investigations carried out to determine the constrictor effect, determined by changes in skin temperature, of intravenous injection of epinephrine before and after sympathectomy. The method is essentially the same as that reported previously by two of us (Fatherree and Allen), who used the electric thermometer described by Sheard. Intra-arterial injections were performed after local anesthetization, and the same precautions of study were observed as when studies were conducted to determine sensitivity to intravenous injection of epinephrine. The degree of completeness of sympathectomy was determined by the sweating test described by Roth, which is based on the observation that, when complete sympathetic denervation has been performed, sweating cannot be induced reflexly. If sweating can be induced reflexly following operation, the sympathectomy is considered incomplete.

COMMENT ON THE SYMPATHETIC FIBERS CUT BY THE VARIOUS OPERATIONS

In the dog vasoconstrictor nerve fibers to the forepaw arise from the fourth to the tenth thoracic segments inclusive. Occasionally such fibers may arise from the third thoracic segment.[24] In the cat preganglionic fibers may also arise from the first thoracic segment to supply the forelimb.[22] Apparently in man the vasoconstrictor fibers of the hands arise from the second to the sixth or seventh thoracic segments respectively.[14] It is possible that some preganglionic fibers arise from the first thoracic nerve, but, if present, they are probably insignificant, since operations which do not disturb sympathetic nerves from the first thoracic segment may completely denervate the hand, a result indicated by absence of reflex sweating.[36, 38]

The important point, however, with regard to the question of whether the preganglionic or the postganglionic fibers, or both, are being cut by an operative procedure is the situation of the ganglia in which the synapses between the preganglionic and postganglionic fibers are made. Langley[24] stated that in the cat these synapses are in the stellate ganglion solely. In man it is more difficult to speak with certainty of the situation of the synaptic junctions of the sympathetic nerves which supply the upper extremity. However, it would appear likely that synapses are made in the middle cervical ganglion as well as the stellate ganglion, since the former ganglion usually is connected through gray rami with the fifth and sixth cervical nerves and, in some instances, also with the fourth and seventh cervical nerves.[21, 30] This probability is borne out by the finding of Foerster

that stimulation of the middle cervical ganglion produces vasoconstriction in the upper extremity of the corresponding side. It appears unlikely that the sympathetic fibers which supply the upper extremity of man make synapses in ganglia other than the middle cervical, the stellate, and the second thoracic.

In the treatment of vasospastic conditions of the upper extremity, currently two main types of operations are practiced; namely, the cervicothoracic ganglionectomy of Adson and the thoracic sympathectomy which was first reported by Telford,[38] and later by Smithwick[36] and still later by Telford again.[39] Cervicothoracic ganglionectomy consists essentially in removal of the stellate and second thoracic ganglia, with the intervening trunk. This operation, therefore, accomplished postganglionic section of all those sympathetic nerves, synapses of which are in either the stellate or second thoracic ganglia. However, the operation accomplishes preganglionic section of any sympathetic nerves to the upper extremity which pass upward through stellate or second thoracic ganglia to synapse in the middle cervical ganglion. Therefore, it would appear likely that cervicothoracic ganglionectomy accomplishes partially a postganglionic section and partially a preganglionic section of the sympathetic nerves which supply the upper extremity of man. It is probable, however, that postganglionic section is predominantly accomplished.

The thoracic type of sympathectomy, as recommended by Telford,[38, 39] consists in section of the thoracic sympathetic chain below the third thoracic ganglion and division of the rami which enter the sympathetic chain from the second and third thoracic nerves. Most likely, this operation accomplishes preganglionic section predominantly, since it is improbable that any considerable number of sympathetic fibers going to the upper extremity make their synapses in the second thoracic ganglion. The thoracic sympathectomy recommended by Smithwick[36] consists in section of the thoracic sympathetic trunk below the third thoracic ganglion, and section of both the anterior and posterior roots of the second and third intercostal nerves within the intervertebral foramina. Theoretically, this operation should result in section of preganglionic fibers exclusively, since the gray rami of the second thoracic ganglion are not cut as they may be in Telford's[38, 39] operation.

In presenting the results of our investigations concerning the effect of epinephrine on the digital arterioles of the upper extremities before and after sympathectomy, therefore, we shall consider that the digital vessels of persons who have undergone cervicothoracic ganglionectomy have been subjected to denervation (postganglionic section) and that the digital vessels of those who have undergone operation of the type recommended by Telford[38, 39] and by Smithwick[36] have been subjected to decentralization (preganglionic section).

The hindlimb of the dog is supplied with vasomotor nerves by the eleventh thoracic to the second lumbar nerves inclusive and, to a less extent, by the third lumbar nerve, according to the investigation of Bradford and Bayliss, originally presented by Langley.[24] In man the vasomotor fibers appear to arise from the ninth thoracic to the third lumbar segments inclusive.[14] As in the upper extremities, however, the important point relative to whether preganglionic or postganglionic fibers are cut is the situation of the ganglia in which the synapses between the preganglionic and postganglionic fibers are made. In the cat the sympathetic nerve fibers to the hindleg make their synapses in the sixth and seventh lumbar and the first sacral ganglia, and a few perhaps in the second sacral ganglion.[24] In man it is probable, in the light of Langley's findings[23, 24] relative to the distribution of postganglionic fibers to the spinal nerves, that the synapses of the sympathetic nerve fibers to the feet are situated, for the most part, in the ganglia which correspond to the spinal nerves which form the sciatic nerve; namely, the fourth lumbar to the third sacral ganglia inclusive. When lumbar sympathectomy is performed, only preganglionic fibers are cut unless the fourth lumbar ganglion is removed, under which circumstance some postganglionic fibers may be excised.

In view of the definite and considerable difference in vasomotor reactions of the upper and lower extremities, as they concern both vasodilation and vasoconstriction,[2, 13, 19] it is probably not safe to compare vasoconstrictor effects of epinephrine in an upper extremity which has been sympathectomized by postganglionic section with vasoconstrictor effects in a lower extremity which has been sympathectomized by preganglionic section, and expect to draw reliable conclusions with regard to the relative constrictor effects of epinephrine on vessels which have been sympathectomized by postganglionic and preganglionic section respectively.

THE CONSTRICTOR EFFECT OF EPINEPHRINE ON DIGITAL VESSELS WHICH HAVE BEEN SYMPATHECTOMIZED BY SECTION OF A PERIPHERAL NERVE

We studied one patient who had undergone complete section of the median nerve at the wrist nine months previously. In the regions corresponding to the sensory distribution of the median nerve, tactile, pain, and thermal sensations were entirely lost and also motor power of the muscles of the hand supplied by this nerve was lost. There was no sweating in response to heating the entire body in the regions depicted in Fig. 1. Sweating was normal in the other hand. The vasoconstrictor effect of epinephrine was distinctly greater in the second finger, which was anesthetic and anhidrotic, than in the normally innervated fingers of the same hand and of the opposite hand. Dale and Richards, and Ascroft previously had noted increased vasoconstrictor effects of epinephrine in the feet of animals following section

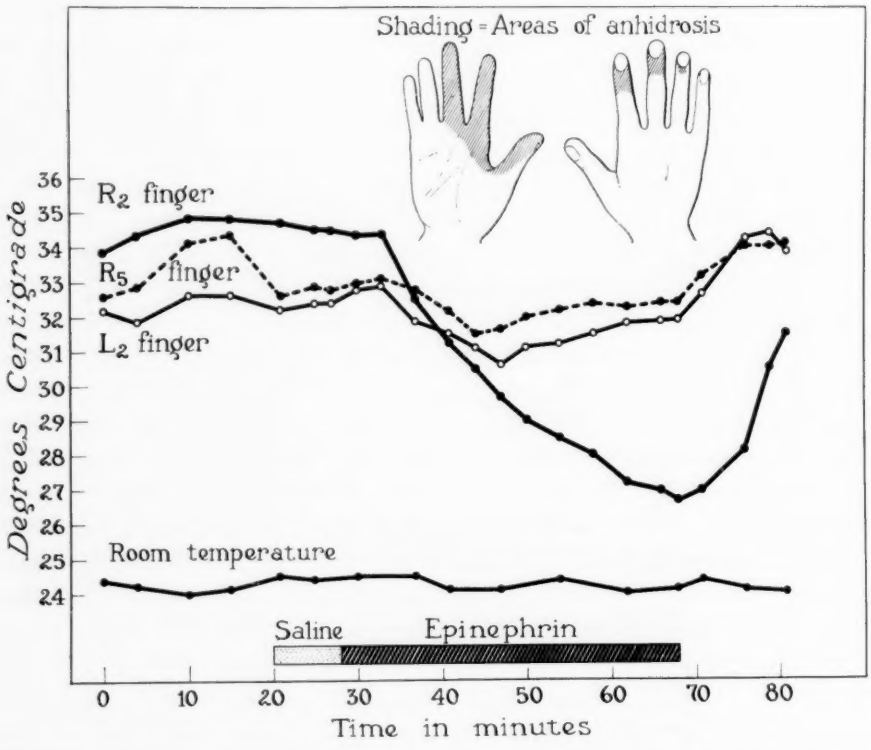

Fig. 1.—Traumatic section of right median nerve; during intravenous injection of epinephrine the temperature of the second finger of the right hand decreased much more than the temperature of the fifth finger of the right hand and the second finger of the left hand.

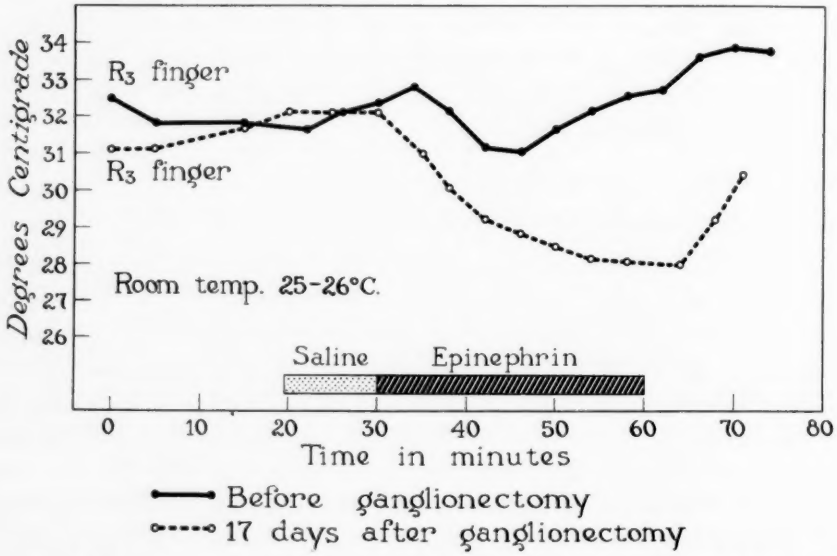

Fig. 2.—Effect of intravenous injection of epinephrine on the temperature of the skin of the third finger of the right hand before and after cervicothoracic ganglionectomy (postganglionic section).

of the peripheral nerves. However, we cannot find a report of this observation having been made previously on man.

THE CONSTRICTOR EFFECT OF EPINEPHRINE ON THE VESSELS SUPPLYING THE FINGERS, BEFORE AND AFTER CERVICOTHORACIC GANGLIONECTOMY (POSTGANGLIONIC SECTION)

We studied the vasoconstrictor effect of epinephrine, administered intravenously, on the digital vessels of five patients before and after cervicothoracic ganglionectomy performed according to the technique of Adson. Our results show that epinephrine produced greater vasoconstriction of the digital vessels of fingers after this type of sympathectomy than it did before the operation was performed (Fig. 2, and Table I). The average decrease in cutaneous temperature in all cases before operation was 1.6° C. and after operation it was 3.7° C. Thus, the magnitude of the decrease in cutaneous temperature after operation was twice that before operation. Sympathectomy appeared complete in all cases except Case 4, which was the only one in which sweating of hands could be induced. In this case mild sweating affected only the volar surfaces of the right third finger and of both wrists. From these studies it would appear that section of the postganglionic components of the sympathetic nerves to the blood vessels of the upper extremity of man does not produce nearly so great an increase in the sensitivity of the smooth muscle of the vessels to epinephrine as this procedure produces in monkeys.[3]

THE CONSTRICTOR EFFECT OF EPINEPHRINE ON THE VESSELS SUPPLYING THE FINGERS, BEFORE AND AFTER THORACIC SYMPATHECTOMY (PREGANGLIONIC SECTION)

Eight cases were studied, six by injecting epinephrine intravenously (Fig. 3 and Table II), and two by the intra-arterial injection of epinephrine. Sympathectomy appeared complete in all but Case 7, which was the only one in which sweating could be induced, and even in this case it could be induced only on the inner aspects of the right arm and forearm, the volar surface of the left forearm, and the left thenar eminence. In Case 6 (Table II) the procedure was bilateral section of the trunk below the third thoracic ganglion, bilateral resection of a proximal segment of the second and third intercostal nerves, and bilateral ramisectomy of the second thoracic ganglion. The procedure to which the patients in Cases 7 and 8 were subjected included bilateral section of the trunk below the third thoracic ganglion and bilateral ramisectomy of the second and third thoracic ganglia. In Case 9 the procedure included bilateral section of the thoracic trunk below the third thoracic ganglion, section of the rami of the second and third thoracic nerves on the right, and section of the second and third intercostal nerves on the left. In Case 10 the procedure included bilateral anterior rhizotomy of the

TABLE I

EFFECT OF INTRAVENOUS INJECTION OF EPINEPHRINE ON THE TEMPERATURE OF THE SKIN OF THE FINGERS BEFORE AND AFTER CERVICOTHORACIC GANGLIONECTOMY (POSTGANGLIONIC SECTION)

CASE	DIAGNOSIS	BEFORE POSTGANGLIONIC SYMPATHECTOMY					AFTER POSTGANGLIONIC SYMPATHECTOMY					
		AVERAGE SKIN TEMPERATURE BEFORE INJECTION OF EPINEPHRINE, DEGREES C.	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION OF EPINEPHRINE, DEGREES C.	RATE OF INJECTION OF EPINEPHRINE, C.C. PER MINUTE	TIME CONSUMED IN INJECTING EPINEPHRINE, MINUTES	ROOM TEMPERATURE, DEGREES C.	AVERAGE SKIN TEMPERATURE BEFORE INJECTION OF EPINEPHRINE, DEGREES C.	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION OF EPINEPHRINE, DEGREES C.	RATE OF INJECTION OF EPINEPHRINE, C.C. PER MINUTE	TIME CONSUMED IN INJECTING EPINEPHRINE, MINUTES	ROOM TEMPERATURE, DEGREES C.	DAYS FOLLOWING SYMPATHECTOMY
1	Raynaud's disease	33.1	1.8	5.0	15	26.0	31.0	3.9	4.4	32	25.0	41
2	Sclerodactylia	32.6	0.8	3.0	30	25.0	33.6	3.1	2.6	30	26.0	17
3	Raynaud's disease	33.2	2.5	2.7	26	24.3	32.5	3.0	2.5	26	25.0	13
4	Sclerodactylia	33.5	0.8	10.0	15	26.0	31.8	3.8	6.6	24	26.0	41
5	Causalgia	33.3	2.0	2.6	40	24.2	34.3	4.8	2.5	40	24.7	15

second and third thoracic nerves, bilateral division of the trunk below the third thoracic ganglion, and bilateral section of the rami of the second and third thoracic nerves. Bilateral section of the rami of the second and third thoracic nerves was the procedure employed in Case 11. Hence, in all instances the section was predominantly or entirely preganglionic. In every instance in which epinephrine was injected intravenously, greater vasoconstriction was produced in the fingers after preganglionic section of the sympathetic fibers by thoracic sympathectomy than before the operation was performed. The average decrease in cutaneous temperatures before operation was 2.6° C. and after operation it was 4.6° C.

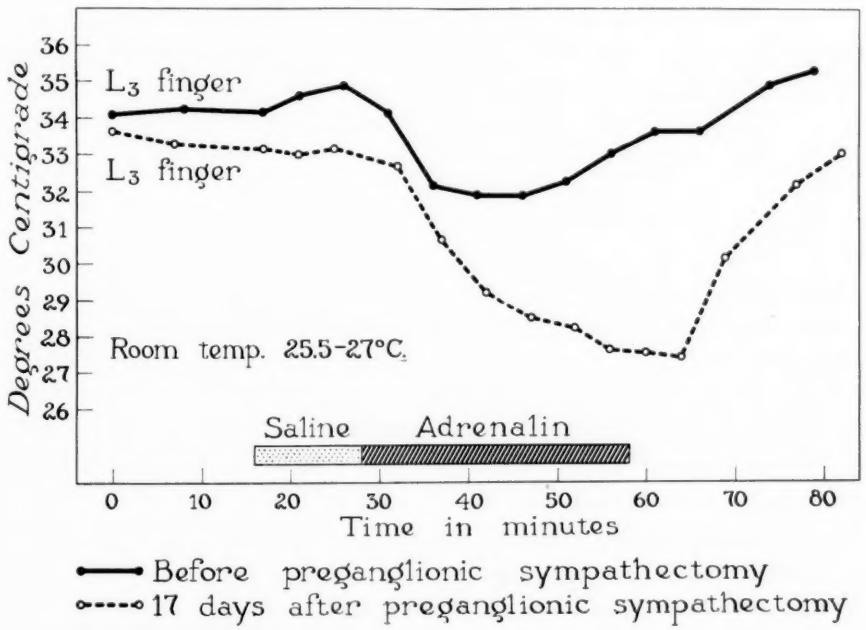

Fig. 3.—Effect of intravenous injection of epinephrine on the temperature of the skin of the third finger of the left hand before and after thoracic sympathectomy (preganglionic section).

Thus, the magnitude of the decrease in cutaneous temperature after operation was approximately twice that before operation. In the two cases in which epinephrine was injected intra-arterially, the operative procedures were similar; they included bilateral division of the main sympathetic trunk below the third thoracic ganglion and bilateral division of the rami of the second and third thoracic ganglia. In one of these two cases the vasoconstrictor effect was slightly greater and more persistent fourteen days after operation than it was before, and in the other case the vasoconstrictor effect was slightly greater before operation.

We have pointed out before that the method of study which we used was not an exact quantitative one. Although the vasoconstrictor effect produced by epinephrine, as indicated by the decrease in cutaneous

TABLE II

EFFECT OF INTRAVENOUS INJECTION OF EPINEPHRINE ON THE TEMPERATURE OF THE SKIN OF THE FINGERS BEFORE AND AFTER THORACIC SYMPATHECTOMY (PREGANGLIONIC SECTION)

		BEFORE POSTGANGLIONIC SYMPATHECTOMY					AFTER POSTGANGLIONIC SYMPATHECTOMY					
CASE	DIAGNOSIS	AVERAGE SKIN TEMPERATURE BEFORE INJECTION OF EPINEPHRINE, DEGREES C.	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION OF EPINEPHRINE, DEGREES C.	RATE OF INJECTION OF EPINEPHRINE, C.C. PER MINUTE	TIME CONSUMED IN INJECTING EPINEPHRINE, MINUTES	ROOM TEMPERATURE, DEGREES C.	AVERAGE SKIN TEMPERATURE BEFORE INJECTION OF EPINEPHRINE, DEGREES C.	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION OF EPINEPHRINE, DEGREES C.	RATE OF INJECTION OF EPINEPHRINE, C.C. PER MINUTE	TIME CONSUMED IN INJECTING EPINEPHRINE, MINUTES	ROOM TEMPERATURE, DEGREES C.	DAYS FOLLOWING SYMPATHECTOMY
6	Raynaud's disease	33.6	2.9	2.7	30	24.6	32.9	4.9	2.7	30	25.0	14
7	Sclerodactylia	32.1	1.0	2.5	30	25.0	32.1	4.0	3.0	30	25.5	18
8	Sclerodactylia	34.3	3.1	4.2	34	27.0	32.3	5.2	3.3	33	25.5	17
9	Raynaud's disease	32.6	1.9	3.0	35	24.5	30.8	2.4	3.7	35	26.0	15
10	Raynaud's disease	33.2	2.3	2.8	35	25.1	34.1	5.4	2.8	35	24.2	105
11	Raynaud's disease	32.9	4.7	2.5	30	25.0	33.0	6.0	2.5	30	24.8	16

temperature, was increased by both operations, postganglionic section did not increase the magnitude of the vasomotor response to the intravenous injection of epinephrine more than preganglionic section did. We do not interpret these results as an indication that there is no difference in the magnitude of the vasoconstrictor effect of epinephrine following preganglionic and postganglionic section, but the results suggest that this is true. Certainly, if such a difference exists in man, it is small, much less obvious than it is in the monkey,[1] and probably of little clinical significance. Simmons and Sheehan recently have studied two patients who had undergone preganglionic section of the sympathetic nerves of one upper extremity and postganglionic section of the other upper extremity. They found that, when epinephrine was administered intravenously, the decrease in cutaneous temperature was greater on the side of the postganglionic section. They pointed out, however, that the difference was not very great.

THE CONSTRICTOR EFFECT OF EPINEPHRINE ON THE VESSELS SUPPLYING THE TOES, BEFORE AND AFTER LUMBAR SYMPATHECTOMY (PREGANGLIONIC SECTION)

Studies such as we are about to report have apparently not been made previously, although Daniélopolu and his associates[10] found that, after unilateral lumbar sympathectomy, sensitivity to intravenous injection of epinephrine was greater on the sympathectomized side than it was on the normally innervated side.

Four patients were subjected to lumbar ganglionectomy according to the technique of Adson (Table III). In all instances sympathectomy was complete. The average decrease in cutaneous temperature resulting from intravenously injected epinephrine was greater after operation than it was before in only two instances (Cases 12 and 13) and in one of these (Case 13) the change was insignificant.

The effects of intra-arterial injection of epinephrine were studied before and after operation in six cases. All but one of these (Case 1) were cases of hypertension. The operation consists of a ganglionic removal of the first and second lumbar ganglia with a division of the trunk between the second and third lumbar ganglia. The postoperative studies were carried out from twenty to fifty-one days following operation. In no instance could sweating of the feet or distal parts of the legs be demonstrated. In only two cases (Table IV, Cases 20 and 21) was the average decrease in temperature of the skin of the toes greater following operation than it was before, and in these cases the differences were not striking. However, in four of five cases persistence of the vasoconstrictor action was remarkably greater following operation than it was before (Table V). An example of this greater persistence of vasoconstrictor effect of epinephrine following sympathectomy is graphically presented in Fig. 4. These results are

TABLE III

EFFECT OF INTRAVENOUS INJECTION OF EPINEPHRINE ON THE TEMPERATURE OF THE SKIN OF THE TOES BEFORE AND AFTER LUMBAR GANGLIONECTOMY

CASE	DIAGNOSIS	BEFORE POSTGANGLIONIC SYMPATHECTOMY					AFTER POSTGANGLIONIC SYMPATHECTOMY					
		AVERAGE SKIN TEMPERATURE BEFORE INJECTION OF EPINEPHRINE, DEGREES C.	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION OF EPINEPHRINE, DEGREES C.	RATE OF INJECTION OF EPINEPHRINE, C.C. PER MINUTE	TIME CONSUMED IN INJECTING EPINEPHRINE, MINUTES	ROOM TEMPERATURE, DEGREES C.	AVERAGE SKIN TEMPERATURE BEFORE INJECTION OF EPINEPHRINE, DEGREES C.	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION OF EPINEPHRINE, DEGREES C.	RATE OF INJECTION OF EPINEPHRINE, C.C. PER MINUTE	TIME CONSUMED IN INJECTING EPINEPHRINE, MINUTES	ROOM TEMPERATURE, DEGREES C.	DAYS FOLLOWING SYMPATHECTOMY
12	Megalocolon	30.6	2.0	4.1	30	25.0	33.6	4.5	2.2	30	24.0	17
13	Raynaud's disease	31.5	3.5	2.7	30	24.6	32.9	3.9	2.7	30	24.7	36
14	Thromboangiitis obliterans	30.1	0.1	5.3	19	26.5	30.8	0.6*	2.3	31	27.0	9
15	Thromboangiitis obliterans	29.0	2.3	2.7	31	24.8	29.5	1.8	2.7	30	25.3	11

*This was not a decrease, but an increase, in cutaneous temperature.

in keeping with those which Elliott[11] obtained in experiments on animals. He found that all smooth muscle contracts with greater persistence in the presence of epinephrine following sympathectomy of preganglionic type.

The findings obtained from the observations just reported indicate that section of the preganglionic components of the sympathetic nerves which supply the toes results in no significant increase in sensitivity of the vessels when epinephrine is injected intravenously or intra-arterially.

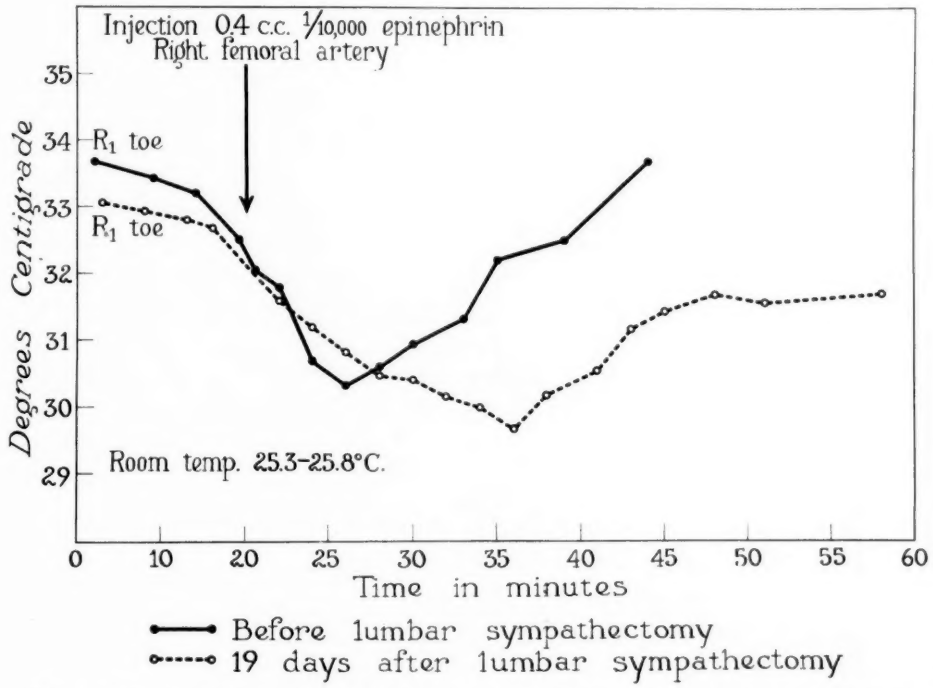

Fig. 4.—Effect of intra-arterial injection of epinephrine on the temperature of the first toe of the right foot before and after lumbar sympathectomy.

THE COMPARATIVE EFFECT OF INTRAVENOUS INJECTION OF EPINEPHRINE ON THE CUTANEOUS TEMPERATURE OF TOES AND FINGERS DENERVATED OF SYMPATHETIC FIBERS

As stated previously, there has been advanced the hypothesis that failure of ganglionectomy (postganglionic section) to cure Raynaud's disease of the hands is due to the great sensitivity of arterioles which results from operation to normally circulating epinephrine, while routine cure of Raynaud's disease of the feet is due to the much less marked increase in sensitivity to epinephrine which results from lumbar sympathectomy (preganglionic section). If this is true, the temperature of the skin of the fingers of the patients who had undergone postganglionic section for Raynaud's disease of the hands ought to decrease much more than the cutaneous temperature of the toes

TABLE IV

EFFECT OF INTRA-ARTERIAL INJECTION OF EPINEPHRINE ON THE TEMPERATURE OF THE SKIN OF THE TOES BEFORE AND AFTER LUMBAR GANGLIONECTOMY

CASE	BEFORE SYMPATHECTOMY				FOLLOWING SYMPATHECTOMY			
	AMOUNT OF EPINEPHRINE INJECTED, C.C. OF 1:10,000 SOLUTION	AVERAGE SKIN TEMPERATURE AT TIME OF INJECTION	AVERAGE DECREASE IN SKIN TEMPERATURE AFTER INJECTION, DEGREES C.	ROOM TEMPERATURE, DEGREES C.	AMOUNT OF EPINEPHRINE INJECTED, C.C. OF 1:10,000 SOLUTION	AVERAGE SKIN TEMPERATURE AT TIME OF INJECTION	AVERAGE DECREASE IN SKIN TEMPERATURE, RESULT	ROOM TEMPERATURE, DEGREES C.
16	0.17	31.7	0.8	25.1	0.17	32.9	0.3	25.7
17	0.29	30.5	1.4	24.9	0.29	33.2	1.1	26.1
18	1.0	33.3	2.5	26.8	1.0	32.8	1.6	25.2
19	0.75	31.8	2.6	25.3	0.75	32.4	2.6	25.3
20	0.40	31.3	1.6	25.3	0.40	32.1	1.9	25.8
21	0.61	31.9	1.7	25.6	0.61	32.1	2.6	25.0

TABLE V

DURATION OF DECREASE IN TEMPERATURE OF THE SKIN OF THE TOES PRODUCED BY INTRA-ARTERIAL INJECTION OF EPINEPHRINE BEFORE AND AFTER LUMBAR GANGLIONECTOMY

CASE	AVERAGE DURATION OF DECREASE IN SKIN TEMPERATURE, MINUTES	
	BEFORE SYMPATHECTOMY	FOLLOWING SYMPATHECTOMY
22	10	24
23	11	24
24	22	27
25	14	22
26	24	10

following preganglionic section for Raynaud's disease of the feet, when epinephrine is injected intravenously. Two observations by Smithwick, Freeman, and White,[37] and White[41] indicate that this is true.

We injected epinephrine intravenously in three cases in which sympathectomy of all four extremities had been performed for Raynaud's disease (Table VI). In two of these cases (Cases 27 and 28) the upper extremities had been denervated by cervicothoracic ganglionectomy and the lower extremities had been denervated by lumbar ganglionectomy. In the third case the upper extremities had been denervated by preganglionic sympathectomy and the lower extremities by lumbar ganglionectomy (Table VI). Sweating tests indicated that lumbar sympathectomy was complete in all instances.

TABLE VI

EFFECT OF INTRAVENOUS INJECTION OF EPINEPHRINE ON THE TEMPERATURE OF THE SKIN OF THE HANDS AND FEET FOLLOWING SYMPATHECTOMY

CASE	ROOM TEMPERATURE, DEGREES C.	INJECTION OF EPINEPHRINE		AVERAGE SKIN TEMPERATURE BEFORE INJECTION, DEGREES C.		AVERAGE DECREASE IN CUTANEOUS TEMPERATURE, DEGREES C.		MONTHS AFTER OPERATION ON	
		RATE, C.C. PER MINUTE	TIME REQUIRED, MINUTES	FINGERS	TOES	FINGERS	TOES	FINGERS	TOES
27	26.0	10.8	17	31.8	34.4	5.3	3.8	13	36
28	27.0	4.2	35	33.7	33.1	4.9	2.8	72	60
29	25.2	2.7	30	32.7	33.4	4.9	4.2	⅔	1

Sweating tests indicated that sympathectomy was complete in all but Case 28 of operation for the relief of Raynaud's disease of the upper extremities. In this case there was slight sweating on the dorsum of a hand. In all instances the average decrease in cutaneous temperature was greater in the fingers than in the toes (including the instance in which preganglionic section had been done). In Case 27 the difference was only 1.5° C.; in Case 28 the difference was 2.1° C. and in Case 29 the difference was negligible. Superficially this would seem to indicate that preganglionic section (Case 29) produced effects on sensitivity more nearly comparable to lumbar ganglionectomy than postganglionic section did (Cases 27 and 28), but in reality sensitivity

in the fingers was about the same in all instances. For some unknown reason sensitivity was greater in the toes in Case 29 than in Cases 27 and 28.

The objection might be raised, in the light of the work of Smithwick and his associates,[37] as a result of which they concluded that the incompletely sympathectomized extremity does not become hypersensitive to epinephrine, that reliable conclusions cannot be drawn from our observations because there was evidence that cervicothoracic ganglionectomy of the upper extremities in some of our cases was incomplete. However, the fingers in all of the cases were completely sympathectomized as was shown by sweating tests; furthermore, sweating, when induced, was minimal, which indicated almost complete sympathectomy.

COMMENT

Our studies indicate that lumbar ganglionectomy (preganglionic section) does not increase sensitivity of the arterioles of toes to epinephrine significantly. It impresses us as fallacious, however, to conclude that this is true, because preganglionic and not postganglionic sympathectomy was performed. It seems much more probable that the increased sensitivity which occurs in the fingers but not in the toes is due to inherent differences in the vasomotor reactions in the fingers and toes.[13, 19, 25]

Both preganglionic section and postganglionic section of the sympathetic nerves to the hands increase the sensitivity of the digital arterioles to intravenous injection of epinephrine, and in about the same degree. The results of our studies are therefore in direct opposition to the results of similar studies by Smithwick and his associates,[37] who found that preganglionic section increased sensitivity of digital arterioles to epinephrine very much less than did postganglionic section. We have no explanation of these divergent results. It may be well to emphasize that the method of study we employed is relatively crude, but the same method was used by Smithwick and his associates. The explanation of Smithwick and his associates, that preganglionic section for Raynaud's disease effected better clinical results than ganglionectomy because the former operation did not greatly increase sensitivity to epinephrine while the latter did so, seems to us to be based, therefore, on insecure evidence. Simmons and Sheehan frankly did not accept the explanation of Smithwick and his associates. Much support would be given the thesis of Smithwick and his associates if preganglionic section routinely cured patients with Raynaud's disease of the upper extremities, but in our experience it does not. Lewis[25] and Simmons and Sheehan have made similar observations. Since sympathectomy cures Raynaud's disease of the feet routinely and does not increase sensitivity of the arterioles to epinephrine, and since

both preganglionic section (Smithwick[36]) and ganglionectomy (Adson) do not cure all patients with Raynaud's disease of the hands and do produce increased sensitivity of arterioles to epinephrine, a logical conclusion might be that all kinds of sympathectomy fail to cure Raynaud's disease of the hands because they cause increased sensitivity in that region, while sympathectomy cures Raynaud's disease of the feet because it does not increase the sensitivity of pedal arterioles to epinephrine. However, there are substantial objections to such an idea.[13, 35] In this connection it might be mentioned that in our experience vasospastic symptoms never develop in the fingers following cervicothoracic ganglionectomy for conditions other than vasospastic disease (for instance hyperhidrosis). Yet, if the digital vessels were as sensitive to epinephrine as has been implied, one would expect this to occur. In fact, we are frankly skeptical that sensitivity of arterioles to epinephrine has anything to do with failure to cure Raynaud's disease of the hands routinely by sympathectomy.

The fact that sympathectomy cures Raynaud's disease of the feet, and fails to do so in some instances of Raynaud's disease of the hands, still puzzles us. If it were because of increased sensitivity to epinephrine, why should some patients with Raynaud's disease of the hands be cured by preganglionic section, whereas some are benefited little or none, and why should some be cured by postganglionic section while some are benefited little or none? There must be other explanations. Some believe that the failure to cure Raynaud's disease of the hands by sympathectomy is due to incomplete operation, yet in such instances the operation seems as complete, as tested by ability of the skin to sweat, as it seems in some instances in which the operation produced complete cure. Moreover, as Simmons and Sheehan have pointed out, if all patients who have had incomplete operations are excluded from consideration, there remain some who reacquire vasomotor disturbances. Also, some patients who seem to have had complete operations are not cured. Furthermore, there is little correlation between clinical results and completeness of operation; an operation that almost entirely denervates the hands occasionally fails almost completely to alleviate symptoms of Raynaud's disease. Lewis has maintained, for almost ten years, that Raynaud's phenomena are not a manifestation of abnormal vasomotor tone but result from local sensitivity of digital arteries to cold. He agreed that sympathectomy is an excellent method of treatment in many instances, but he expressed the belief that the good results of operation are due to relief of normal vasomotor tone and not to relief of abnormal vasomotor tone. His expressed belief is that the central sympathetic nervous system has nothing to do with Raynaud's disease. However, his thesis does not explain cure by sympathectomy of the feet and failure of cure in some instances by sympathectomy of the hands. More-

over, as Simmons and Sheehan pointed out, Lewis'[25] thesis does not explain why vasomotor symptoms in the hands may be abolished by sympathectomy and then recur. Other observations may be pertinent. Raynaud's disease of the feet is mild and cured by sympathectomy. Raynaud's disease of the hands occurs more commonly than Raynaud's disease of the feet and is usually more severe and occasionally is not cured by sympathectomy. Is occasional failure of operation to cure Raynaud's disease of the hands due to the fact that it is more severe than Raynaud's disease of the feet? Is the fact that under ordinary circumstances the hands undergo greater exposure than the feet also a factor? No completely acceptable explanation is now available for failure of operation to cure some instances of Raynaud's disease of the hands while operation routinely cures Raynaud's disease of the feet. Certainly, it now seems definitely true that preganglionic section does not uniformly cure Raynaud's disease of the hands and that it does not cause much less increase in sensitivity of the digital arteries to epinephrine than does ganglionectomy. What appeared to be a pleasant solution of a problem has been reexamined and found to be of uncertain value. Whatever the problems connected with it may be, sympathectomy is the most satisfactory method of treatment of Raynaud's disease.

CONCLUSIONS

1. Both preganglionic section and postganglionic section for Raynaud's disease of the hands caused increased sensitivity of digital arteries to epinephrine, but the degree of increased sensitivity was about the same in both instances.

2. Sympathectomy for Raynaud's disease of the lower extremities did not significantly increase sensitivity of digital arterioles to epinephrine.

3. The problem of unsatisfactory results that occasionally follow operation for Raynaud's disease of the hands has not been satisfactorily solved by a study of sensitivity of digital arterioles to epinephrine.

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A CONSIDERATION OF THE VALUE AND INDICATIONS FOR ENCEPHALOVENTRICULOGRAPHY, WITH ESPECIAL REFERENCE TO ITS USE IN BORDERLINE NEUROSURGICAL CONDITIONS*

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INTRODUCTION

THE withdrawal of cerebrospinal fluid, either by ventricular puncture or by lumbar puncture, and the immediate replacement of the fluid by air is now a widely used method in the neurosurgical armamentarium. For this, we are indebted to the studies and communications furnished by Dandy[1] in 1918 and 1919. We shall not, however, be particularly concerned with its use as a corroborative aid in patients who are almost certainly harboring tumors, but in whom there is insufficient clinical evidence to indicate the exact extent of the lesion. There are, nevertheless, many conditions in which encephalography or ventriculography is of great aid; first, in establishing the diagnosis, and second, in determining whether a major craniotomy is necessary or warranted. Such patients come under the general group of "brain tumor suspects" and it is our intention to emphasize the importance of air injections whenever reasonable doubt exists as to the diagnosis of patients in this category. Five groups have been selected in which air injections of one kind or another are used either to establish the proper diagnosis or to indicate or contraindicate the necessity for a major operation. These groups are: (1) psychiatric cases, (2) cerebral vascular disease, (3) post-traumatic sequelae, (4) arachnoiditis and other inflammatory lesions, and (5) epilepsy. Before proceeding to a discussion of the groups mentioned, a brief review of the indications for these procedures as given by other writers will be helpful.

Indications For and Uses of Encephalography.—Encephalography is a procedure in which a series of properly exposed roentgenograms are made of the head in several positions, usually in the erect posture, immediately after the removal of all the available cerebrospinal fluid and its replacement with air by the lumbar route.[2]

It is never advisable to use this method in the known presence or even in definite suspicion of increased intracranial pressure, the tendency for the cerebellum to be drawn downward through the foramen magnum causing pressure upon the medulla and ultimate respiratory paralysis in such cases being too well known to be commented upon.*

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*It is scarcely necessary to add that a Queckenstedt test should rarely, if ever, be performed in the course of an ordinary lumbar puncture or in encephalography as it is of value only in the diagnosis of intraspinal lesions.

The literature is replete with the use of this method in innumerable neurological and neurosurgical conditions. Articles by Pendergrass,[2] E. Myer,[3] Adson,[4] Pancoast,[5] Grant,[6] Friedman,[7] Wechsler and Gross,[8] and Frazier,[9] among others, stress its value in the diagnosis of the nature of the essential lesion in cases of epilepsy; intracranial post-traumatic conditions; congenital lesions of the brain; birth injuries; atrophic, inflammatory, and degenerative affections of the brain; unexplained headache; and psychoneurosis.

Pendergrass[2] quotes Pancoast and Fay who found 1.2 per cent mortality in 1,529 cases of encephalography.

Not all writers on the subject agree that encephalography should be used only in those cases which do not have increased intracranial pressure. Gardner (quoted by Pendergrass[2]) performs encephalography in all cases of obscure intracranial lesions, with or without demonstrable increased pressure, clinically, except those having suspected posterior fossa lesions (a clinical differentiation which it is often difficult if not impossible to make). We cannot agree with this view for the reasons previously stated.

In summarizing the indications and uses of encephalography, as contained heretofore in the literature, most writers on the subject agree that its widest field of usefulness is in the differential diagnosis of various types of epilepsy, post-traumatic and congenital lesions, inflammatory and degenerative affections, and obscure neurological disorders in which there is no evidence of increased intracranial pressure. To this general statement might be added an additional rule employed by us, which limits the application of the procedure still further; namely, to withhold encephalography if the patient is over 50 years of age; ventriculography is probably better in more elderly individuals whether increased intracranial pressure is demonstrable clinically or not, as the latter procedure, even in patients without increased intracranial pressure, is associated with considerably less "reaction" than is encephalography.

Indications For and Uses of Ventriculography.—Ventriculography is a procedure in which a series of properly exposed roentgenograms are made of the head in several positions, usually in the horizontal posture, immediately after the removal of cerebrospinal fluid directly from the ventricles of the brain and its replacement by air.[2]

Ventriculography is the procedure of choice in obscure intracranial conditions in which there is evidence of increased intracranial pressure as shown chiefly by haziness or elevation of the optic disks, although it is well known that in 15 to 20 per cent of mass lesions of the brain there is no elevation of the optic nerve heads at any stage of the disease. However, in any series of encephalograms, or even in patients submitted to ordinary lumbar puncture, the great majority of the fatalities which result after the use of these procedures occur in pa-

tients who are harboring a brain tumor or other mass lesion, most of whom show some elevation of the disks. Therefore, in any patient in whom diagnosis is obscure, be it post-traumatic epilepsy, a probable inflammatory lesion, a tumor suspect, etc., if there be any evidence, by clinical examination or by ordinary roentgenograms of the skull, that there is increased intracranial pressure, it is much the safer procedure to use ventriculography rather than encephalography.

Many writers have previously discussed the use of ventriculography in borderline neurosurgical conditions. Among them are De Martel, Guillaume, and Paret-Raymond,[10] Vincent, David, and Puech,[11] Foerster,[12] Wanke,[13] Dahl-Inerson,[14] Pendergrass,[2] Riggs,[15] Grant,[16] and Frazier and Gardner.[17]

Frazier[17] rightly observed that, although more deaths have been attributed to ventriculography than to encephalography, it is not proper to compare the mortality statistics of these two procedures because ventriculography is or should be reserved for patients who have increased intracranial pressure, who are, therefore, greater operative risks. He believed that a spinal fluid pressure reading in the horizontal position over 260 mm. of water was a contraindication for encephalography and an indication for ventriculography. The writer suggests that an even lower reading (175 mm. of water in a relaxed patient under local anesthesia in the horizontal position) should be regarded as a "top normal" figure, beyond which encephalography is unsafe.

Pendergrass[2] quotes Grant[16] as stating that the mortality from ventriculography as a single operative procedure in 392 cases from various clinics is 8.2 per cent. However, it is only fair to state that Grant's statistics were compiled in 1923, at a time when our present knowledge of how and when to do air studies was not well established. At that time it was not uncommon to wait several days after a ventriculogram which indicated a tumor or other mass lesion, before proceeding with craniotomy, a procedure now realized to be highly fatal in its tendencies. Pendergrass[2] also states that Dandy believes that only 40 per cent of brain tumors can be localized by neurological examination; whereas, Frazier believed that 60 to 70 per cent could be localized without resorting to an air injection.

In summarizing the indications for and uses of ventriculography as contained heretofore in the literature, it is generally agreed that the main value of the procedure is in the localization of a tumor or other intracranial mass lesion in the presence, usually, of increased intracranial pressure or to obtain a more exact localization than can be made by neurological studies. It cannot be emphasized too often or too vigorously that if such air injection indicate a mass lesion, in the presence of increased intracranial pressure, further operation for the removal of the lesion should be carried out on the same day, if at all possible. Even with this rule in use, the mortality rate of ventricu-

lography will probably always be greater than that of encephalography because of the added risk unavoidably present in cases of increased intracranial pressure.

The following groups of cases are presented to illustrate certain indications for the use of air injections in patients who present difficult diagnostic problems clinically. In some instances the procedure determines the necessity for further operation and finally, it is demonstrated how, in many cases, the air injection is the deciding factor in the management of the case.

I. PSYCHIATRIC CASES

CASE 1.—*Patient with a doubtful tumor history and neurological findings. Pituitary tumor suspect. Ventriculogram normal. X-ray treatment of pituitary gland instituted. Case tentatively classified as intracranial tumor suspect or neurosis.*

Mrs. M., aged 30 years, a widow, was admitted Nov. 21, 1933, complaining of headache and failing vision with transitory amaurosis lasting one minute or less, which had begun three months before admission. The menses were irregular for four months previous to admission. She was referred as a possible case of pituitary tumor. The sella by x-ray was slightly enlarged although the general examination suggested a functional disability. Visual fields revealed so-called tubular vision. Ventriculography was resorted to and the ventricular system was found to be normal. Subsequently, her vision was greatly improved and she was discharged with a provisional diagnosis of a possible pituitary tumor or parasellar lesion. The alternative diagnosis was hysteria. Seven months later she returned to the hospital with headache and bilateral paracentral scotomas with no change in the sella as seen by x-ray. Deep x-ray therapy to the pituitary region was advised and she was again discharged.

Two years after the ventriculogram the patient stated she still had headaches, but neurological examination was essentially negative.

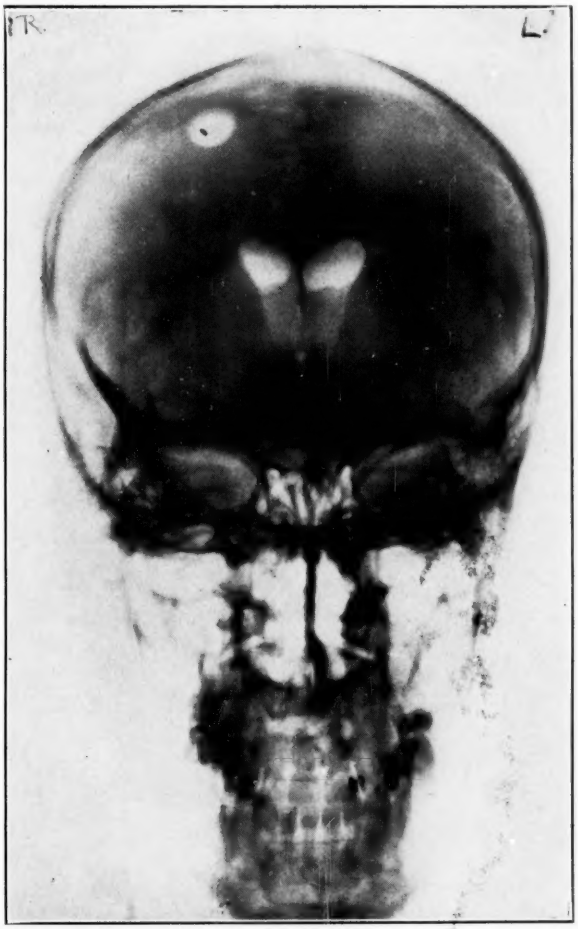
Comment.—This case demonstrates the value of ventriculography in ruling out a brain tumor at the time the patient is under observation. In retrospect it might perhaps have been more informative to have made an encephalogram chiefly because a view of the basilar cisternae would have been of greater value in demonstrating a lesion in this region. This might have been carried out at a later date, but her follow-up report two years after ventriculography would make this seem unnecessary.

CASE 2.—*Occipital headache of three months' duration. History of slight head injury two years before. Unsteady gait. Cerebellar tumor suspect. Ventriculogram showed a normal ventricular system. Tentative diagnosis: hysteria; tumor suspect.*

Miss W., aged 35 years, single, was admitted July 28, 1933, complaining of occipital headache of three months' duration and constant vomiting for five days. Vision was subjectively normal. Two years before admission, there had been a slight injury to the head in an automobile accident. On examination, there was persistent nystagmus to right and left and upward. The left optic disk was slightly edematous. The abdominal reflexes were absent and the gait was unsteady. Visual fields were normal. A cerebellar or pontile tumor was suspected and multiple sclerosis was also considered. Ventriculography revealed a normal ventricular

system (Figs. 1, 2, and 3). Further questioning revealed the fact that there was a marked social maladjustment and also that the patient had worked with a girl who later developed and died of a brain tumor. She was discharged with a tentative diagnosis of multiple sclerosis or possibly a pontile tumor.

Follow-up examination could not be obtained.



Figs. 1, 2, and 3.—Case 2. Normal ventriculograms. These films may be considered a model for comparison with subsequent films. Notice in Fig. 1 that the normal butterfly shape is quite apparent and the size of the ventricles is within normal limits.

Comment.—Ventriculography was undertaken in this instance largely because of headaches, vomiting, and edema of the left optic disk and because the whole clinical picture did not fit in with typical multiple sclerosis. The findings previously mentioned may possibly indicate a beginning posterior fossa tumor, but certainly the ventricular and clinical evidence, to date, is too equivocal to warrant subjecting the patient to a major surgical intracranial procedure. One is certainly justified in pursuing a policy of "watchful waiting" with fairly frequent clinical check-up examinations in such a case; whereas, if the ventricular system had shown marked generalized dilatation, a sub-

occipital exploration would have been undertaken at once with the probable demonstration of a cerebellar tumor.

CASE 3.—*Patient with headache, hypersomnia, and emotional instability. Frontal lobe tumor suspect. Normal ventriculogram. Discharged improved. Tentative diagnosis: probable functional neurological disorder.*

Miss K., aged 26 years, a clerk, was first admitted Sept. 30, 1932, complaining of headaches. The blood pressure was 160/110, but, as there was no evidence of hyperthyroidism, for which she was referred to the clinic, she was sent back to her family physician for further observation. She was readmitted in February, 1933, complaining of hypersomnia, emotional and personality changes. A frontal lobe

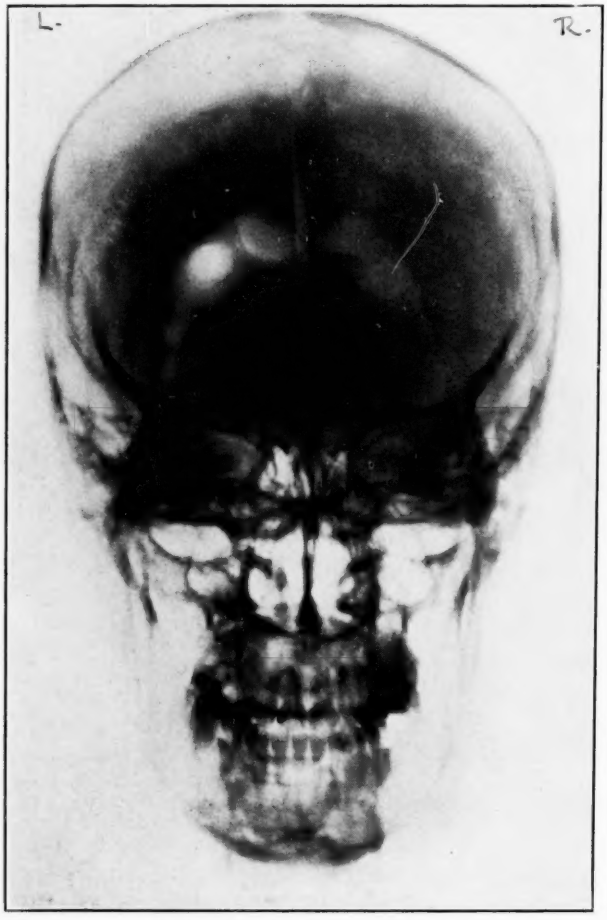


Fig. 2.—See Fig. 1 for legend.

tumor was tentatively considered. At another hospital the impressions had been narcolepsy or hysteria. On March 4, 1933, a ventriculogram was performed which revealed normal ventricles. She was discharged six days later, having had no periods of hypersomnia or other untoward symptoms while in the hospital. She was still classified as a brain tumor suspect but with the probability that she had a neurosis.

The patient's mother reported by letter, March 16, 1939, that the patient appears to be quite well since leaving the hospital, six years previously. She is active in club work and drives her automobile on long trips without becoming unduly tired.

Comment.—It is impossible to rule out a brain tumor (without air injection) in a patient whose dominant symptoms are mental or psychiatric unless the whole clinical picture conforms to a well-recognized psychosis. Latent or unrecognized atypical encephalitis may be the cause of this patient's disability, although her present well-being almost certainly establishes the diagnosis as a neurosis. On the other hand, innumerable cases of frontal lobe or diencephalic tumor have had more or less the same clinical picture as this patient presented and many cases of frontal or interbrain (diencephalic) tumor, especially in children, have been treated as "encephalitis" or neurosis with disastrous results. Careful judgment must be exercised as to the advisability or justification of air studies in patients with mental symptoms alone.

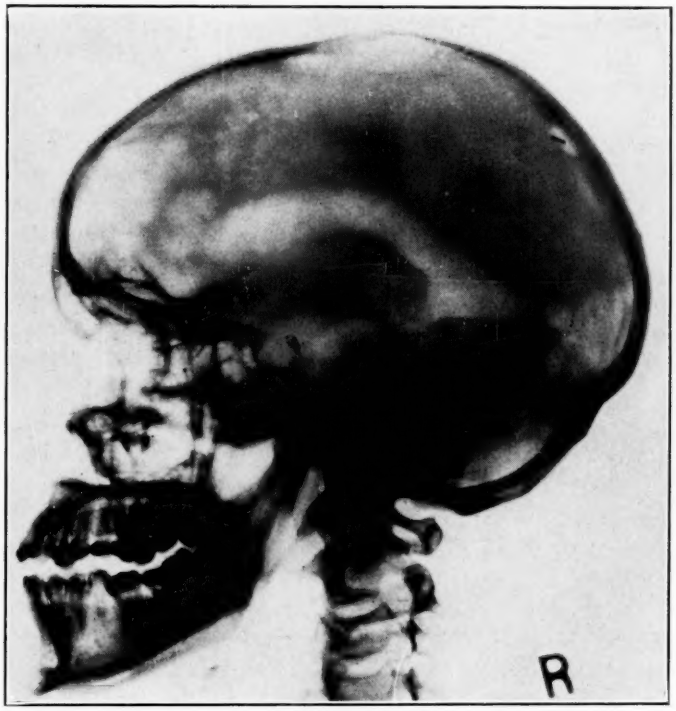


Fig. 3.—See Fig. 1 for legend.

II. CEREBRAL VASCULAR LESIONS

CASE 4.—*Convulsive seizures involving the left side of the body. Neurological examination negative. Ventriculogram normal. Death ten days after ventriculography. Post-mortem: no intracranial mass lesion. Marked arteriosclerosis. Incidental primary carcinoma of bronchus with no demonstrable metastases to any other part of the body.*

Mrs. D., aged 62 years, housewife, was first admitted June 8, 1933, complaining of cough and loss of weight. Two weeks before admission she had fainted; she had also suffered from vertigo. The patient presented clinical evidence of hyperthyroidism and a first stage thyroidectomy was performed on Aug. 14, 1933.

She was readmitted on Oct. 3, 1933, with a complaint of convulsive seizures of the left side. Neurological examination did not reveal anything of significance. A ventriculogram was performed which demonstrated no definite signs of tumor. She became irrational and died ten days after the air study. Post-mortem examination showed no cerebral lesion other than rather marked arteriosclerosis, but a primary carcinoma of the bronchus was discovered which apparently had not metastasized to any other organ.

Comment.—Cerebral vascular lesions notoriously imitate intracranial tumor in the symptoms which they produce, a fact emphasized by Horrax.[18] Convulsive seizures, hemiplegia, hemianopsia, stupor, etc., all can occur equally well with one or the other pathologic entity. The most astute clinician cannot always be sure as to the type of lesion present without actual visualization of the ventricular system. In the case just described, encephalography might have been done, but the patient's age precluded it. The primary carcinoma of the bronchus had nothing to do with the cerebral symptoms.

CASE 5.—*Aphasia and numbness of the right arm. Skull x-ray suggestive of meningioma. Patient discharged without air injection as a probable vascular lesion. Readmitted with paresis of right face and arm. Ventriculogram demonstrated no mass lesion (moderate generalized ventricular dilatation). Presumptive diagnosis: cerebral arteriosclerosis with thrombosis of the left middle cerebral artery.*

Mr. U., aged 65 years, retired, was admitted Jan. 26, 1933, complaining of aphasia and numbness of the right arm of three months' duration. There was tenderness over the left parietal area and x-ray of the skull showed abnormal vessels in the left parietal region suggesting a meningioma. The fundi were normal. A ventriculogram was not thought necessary and the patient was discharged because the weight of evidence appeared to favor a vascular lesion (thrombosis).

He was readmitted on May 17, 1933, at which time he showed euphoria, right facial palsy, and paresis of the right arm. Visual fields were normal. There was a history of violent seizures during which he attacked members of his household and attendants. A ventriculogram was performed which revealed generalized moderate ventricular dilatation (Fig. 4), probably due to cerebral atrophy incident to arteriosclerosis. He was discharged to his home; the presumptive diagnosis was cerebral arteriosclerosis with concomitant thrombosis of the left middle cerebral artery.

Follow-up report, February, 1934: Patient was seen and examined. His condition was the same as at the time ventriculography was performed. There was no evidence of an expanding intracranial lesion.

Comment.—The definite organic signs which this patient had, aphasia, paresis of the right face and arm, and numbness of the right arm, together with x-ray evidence of abnormal vessels in the left parietal region suggestive of a meningioma, certainly warranted an air injection to rule out a tumor or other intracranial mass lesion. His age again precluded an encephalogram which might, otherwise, have been considered in the absence of demonstrable clinical signs of increased intracranial pressure. The generalized ventricular dilatation, together with the euphoria, vio-

lent seizures, and other mental symptoms, supports the presumptive diagnosis previously stated.

III. POST-TRAUMATIC SEQUELAE

CASE 6.—*Post-traumatic headache and vertigo. Encephalography failed to outline ventricles. Ventriculogram carried out later revealed a normal ventricular system. Diagnosis: post-traumatic encephalopathy.*

Mr. A., aged 24 years, single, was admitted Dec. 1, 1932, complaining of vertigo and headache following a head injury in April, 1932, at which time he is said to have sustained a skull fracture. Examination on admission showed nystagmus to right

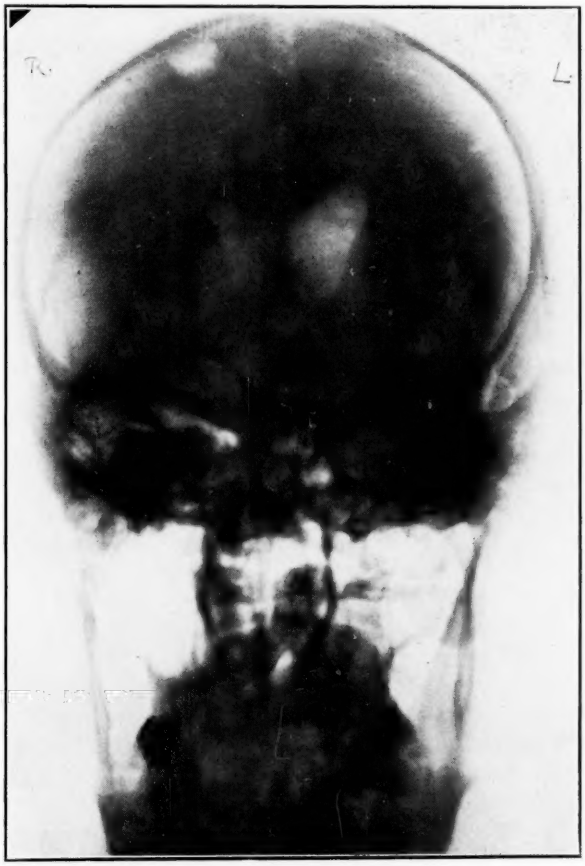


Fig. 4.—Case 5. Ventricles somewhat dilated. Observe that there is no ventricular distortion to suggest a left cerebral mass lesion, but the left ventricle is drawn upward on the side of thrombosis (left). Ventricular dilatation is common in cerebral atrophy incident to arteriosclerosis.

and left. The optic disks were slightly edematous. The impression at this time was that of an old head injury with probable midbrain or pontile contusion. He was discharged and advised to take mild sedatives for his headaches.

He was readmitted on July 13, 1933, complaining of headache and vertigo. Encephalography showed considerable air scattered over the cortex but no ventricular air. There were no areas of localized cerebral atrophy.

He was seen again in September, 1933, at which time he stated that the headaches were still severe. Ventriculography was recommended chiefly to rule out a sub-

dural hematoma; this revealed a normal ventricular system. He was discharged eight days later with the headache and vertigo considerably relieved.

Follow-up report, November, 1936 (three years after the ventriculogram): Patient now having "spells" with loss of consciousness. Slight hemihypesthesia of right side. Another air study advised but refused.

Comment.—This patient was first seen eight months after the original cerebral trauma. No localizing signs were present on examination. Encephalography was preferred, not only for diagnosis but also for its therapeutic effect. In this case the ventricles were not outlined, so recourse was had at a later date to ventriculography, chiefly to rule out a subdural hematoma. This revealed a normal ventricular system and one is thereby assured of not overlooking an intracranial mass lesion.

CASE 7.—*Post-traumatic headache. Encephalogram interpreted as within normal limits. Temporary relief. Ventriculographic procedure revealed a left subdural clot in the course of making the burr opening; ventricular shift to the right side. Headache again relieved. Later, a left subtemporal decompression performed with release of xanthochromic fluid.*

Mr. T., aged 47 years, married, was first admitted in March, 1933, complaining of constant headache which began after a head injury fourteen months before admission to the Clinic. At the time of injury there was also a left facial palsy as well as weakness and tingling of the left forearm and hand. Examination at the Clinic was negative and an encephalogram was made. He experienced great relief but returned five months later, in August, 1933, with a recurrence of the headache. Bilateral ventriculography was performed as the previous encephalography had not been entirely satisfactory and this revealed a subdural liquid collection of old blood on the left side which was drained through the ventriculogram opening. The anteroposterior view (Fig. 5) clearly showed the slight indentation and deviation to the right of the left lateral ventricle with compensatory slight relative dilatation of the right lateral ventricle caused by the left-sided subdural collection. The headache was again relieved. He was readmitted for the third time in February, 1934, with recurrence of the headache and a left subtemporal decompression was performed. On opening the dura, there was an outpouring of fluid under marked pressure from the subdural space. It was faintly xanthochromic. The arachnoid over the sylvian vessels was thickened and gray. He made a rapid convalescence and left the hospital twelve days after operation, feeling quite well.

Follow-up report, November, 1934: Patient's headaches recurred a few months after decompression. He was rapidly declining but was unable to come back for possible further treatment.

Comment.—The finding of a subdural hematoma on the left side in the course of doing the ventriculogram was a fortunate occurrence. In most clinics ventriculography is done through posterior parietal or occipital burr openings and, occasionally, a clot may be missed, as its posterior margin may not extend so far posteriorly. Coleman[19] believes that the best location in searching deliberately for a subdural clot is in the superior temporal region; whereas, Horrax[20] and Horrax and Poppen[21] make incisions in the parieto-occipital region. In Peet's clinic,[22] ventriculography is done routinely at Keen's point just above

and posterior to the ear where an unsuspected clot would almost certainly be found in the course of making a ventriculogram. Peet knows of no subdural hematoma that has been missed in his clinic because the ventriculogram burr opening was placed too far posteriorly. The point to be emphasized is that an osteoplastic flap for the evacuation of a subdural hematoma in a comatose patient may well result fatally; whereas, simple drainage through a burr opening may result in cure.

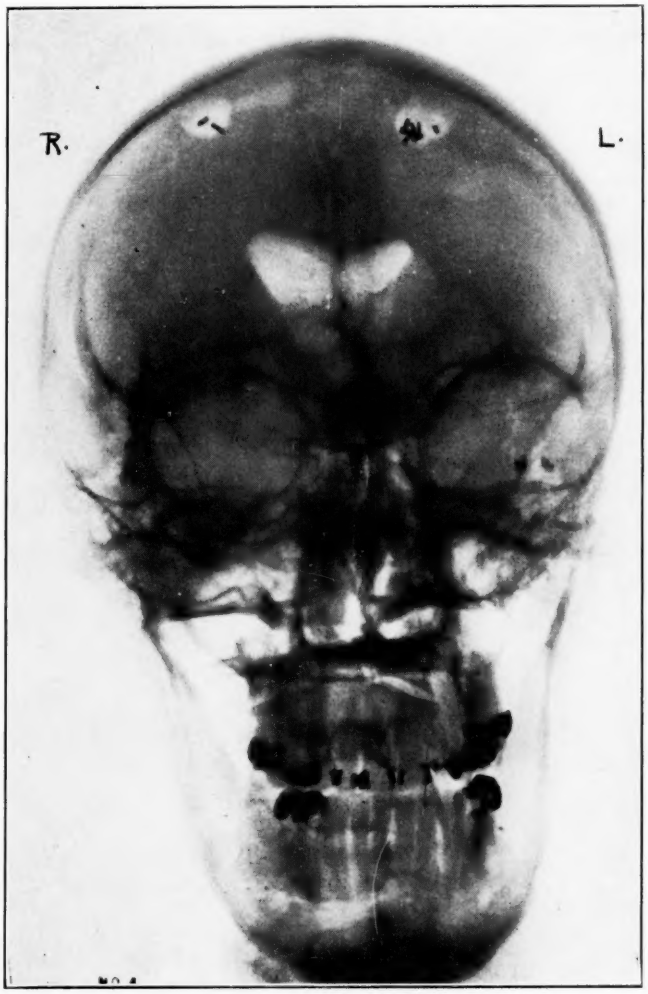


Fig. 5.—Case 7. Note the slight depression of the left lateral ventricle compared with the right and the very slight but definite shift of the entire ventricular system to the right caused by the left subdural clot.

If the ventriculogram burr opening discloses no clot, ventriculography must be performed, followed by an osteoplastic flap, when indicated, in the absence of any traumatic history. We have (December, 1936) had such an experience in another patient. The clot unfortunately did not extend quite far enough posteriorly to the point of the ventriculogram burr opening. The patient was unconscious and in

poor condition. There was no history of trauma. A ventriculogram was performed and the plates showed a shift to the right as in a left cerebral mass lesion. Immediate craniotomy disclosed an enormous liquid subdural hematoma which was evacuated and drained, but the patient succumbed two days later without ever having regained consciousness. Another similar case has been reported recently.[23] In view of these experiences, it would seem advisable, in similar obscure cases, to perform ventriculography at Keen's point, at which site an entirely unsuspected subdural clot would almost certainly be uncovered and could probably be evacuated through the simple burr opening made in the course of the intended ventriculogram.

Figs. 6 and 7.—Case 8 Normal ventricular system except for slight dilatation of the third ventricle (Fig. 6).

In the case described above (Case 7), a left subtemporal decompression was performed six months after the evacuation of the clot because of persistence of headache due to the pent-up subdural fluid and consequent disturbance of the cerebrospinal fluid circulation. We have (1937) had an exactly similar experience.

The cause of the patient's rapid decline (at last report) is obscure unless it be due to cerebral atrophy and degeneration incident to the patient's rather severe head injury originally sustained in 1932.

CASE 8.—*Patient with post-traumatic personality changes and possible manic-depressive psychosis. Brain tumor suspect (? frontal lobe). Encephalogram normal (slight dilatation of third ventricle). Slight depressed fractures of the vault. Discharge diagnosis: Probable manic-depressive psychosis with post-traumatic cerebral injury.*

Mr. T., aged 18 years, a shoe salesman, was admitted Nov. 27, 1933, complaining of nervousness following a head injury six years previously, at which time he was unconscious for five days. For the last three years there had been definite personality changes. Examination suggested a possible manic-depressive psychosis in addition to post-traumatic sequelae. Brain tumor of one or the other frontal lobes

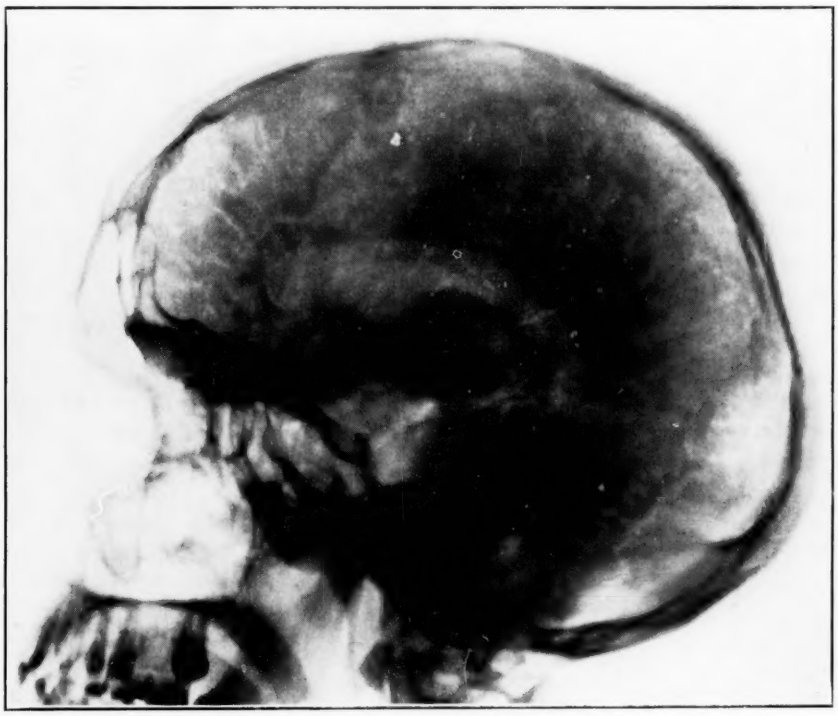


Fig. 7.—See opposite page for legend.

was a more remote possibility. Encephalography was advised. The plates were normal (Figs. 6 and 7) except for slight dilatation of the third ventricle in the anteroposterior view (Fig. 6) and slight depressed fractures of the right parieto-occipital and left parietal areas. These findings were considered to have little or no surgical significance. He was discharged with a diagnosis of manic-depressive psychosis, post-traumatic cerebral injury, and slight depressed fractures of the vault.

Letters to the patient and to his doctor one year later were not answered.

Comment.—To have operated upon this patient's slightly depressed fractures would have been an irrelevant and undesirable procedure as it almost certainly would have accomplished no good and might have

resulted in his ascribing all his disability to the fractures with the possibility of his developing a "fixation complex" concerning them. The case probably represents a post-traumatic syndrome, engrafted on an individual of the constitutionally psychopathic inferior type. Such patients (as Cases 1, 2, and 3) can be eliminated from the tumor group only by an air injection. Even if air studies be interpreted as normal, such patients should be re-examined at frequent intervals thereafter to rule out a surgical lesion. Perhaps the greatest value of air injections, apart from exact localization of a mass lesion, is in such problem cases as the one just described, in determining, for the time being, whether or not a tumor or its equivalent is present.

IV. ARACHNOIDITIS

CASE 9.—*Failing vision, mild frontal headache, and high choked disks. No objective localizing signs. Ventriculogram normal. Right subtemporal decompression to relieve the choking revealed a large subarachnoid fluid collection as the cause of the increased intracranial pressure. Considerable subsidence of the choked disks before discharge.*

Mrs. M., aged 31 years, housewife, was admitted May 4, 1934, complaining of failing vision of three months' duration. There was mild transient headache across the frontal region. Neurological examination was negative except for bilateral choked disks of 5 to 6 diopters. Ventriculography was performed: the plates were interpreted as within normal limits (Fig. 8). Because of the high grade of choked disks and headache, a right subtemporal decompression was performed the same day. When the dura was opened, a great excess of fluid was released from the subarachnoid space. The sylvian vessels were not displaced and the convolutions appeared normal. Eight days after operation the optic disks appeared greatly improved. She was discharged nine days postoperatively with headache relieved and the haziness of vision having completely disappeared.

It is presumed that this patient had no tumor; first, because there was definite evidence at operation of a chronic arachnoiditis of sufficient degree to explain her symptoms, and second, because, if a tumor had reached such proportions as to have caused so high a degree of choking, there would almost certainly have been some dilatation or distortion of the ventricular system as demonstrated by ventriculography.

Follow-up examination, March, 1935: The patient had improved in all respects since decompression. Her fundi showed no elevation of the optic disks; only occasional mild headaches occurred.

Comment.—If the ventriculogram be normal in the presence of choked disks, a subtemporal decompression is always indicated to relieve pressure and preserve vision. If the case be that of an early tumor, localizing symptoms will probably develop later and vision will have been preserved in the meantime. In this case the result following decompression almost certainly removes the case from the "tumor suspect" group, for the rapid subsidence of the choking after release of the fluid argues against tumor and suggests that the pent-up fluid was the major, if not the only, cause of the patient's disability.

CASE 10.—*Prolonged left-sided mastoid infection (mastoidectomy). Bilateral choked disk (3½ diopters) of several weeks' duration. Brain abscess suspect. Normal ventriculogram. Recession of choked disks without further operation. Diagnosis: post-mastoiditic arachnoiditis.*

Miss M., aged 12 years, a school girl, was admitted May 14, 1934, with a long history of mastoid infection on the left side necessitating three operations elsewhere, with subsequent development of choked disks (5 diopters) which suggested the possibility of a brain abscess. On admission to the Clinic she showed 3½ diopters' elevation of the disks. The preoperative note (Dr. Horrax) stated that,

Fig. 8.—Case 9. Ventricular system within normal limits. Because of the high grade of choked disks, subtemporal decompression was performed immediately after ventriculography with release of a large amount of subarachnoid fluid and rapid subsidence of the papilledema.

although there possibly was a brain abscess, the lesion was more likely to be an arachnoiditic process following mastoiditis. The ventriculogram made two days after admission was normal. Thereafter, the fundi receded to 1 diopter elevation within one month after the operation.

Follow-up examination, December, 1935 (one and one-half years after ventriculography): She has been perfectly well in every way and stands at the top of her class in school. She is active in all sports. The optic disks are normal.

Comment.—This child was in remarkably good condition, as was the patient in Case 9, when first seen. She was quite conscious and mentally alert. There was no headache and it was not until the fundi were examined that serious trouble was suspected. The normal ventriculogram definitely ruled out a mass lesion in the cerebrum or cerebellum; this was confirmed by the follow-up examination one and one-half years later. The subsidence of the choked disks after release of fluid from the ventricles may be explained by a shift in position and volume changes in the brain resulting therefrom, bringing about a better cerebrospinal fluid circulation. If the disks remain definitely elevated after release of fluid from normal ventricles for more than a few weeks at most, a subtemporal decompression must be resorted to, primarily for preservation of vision. Arachnoiditic reactions (pseudotumor) following mastoiditis and other infections are not unusual in neurosurgical practice. An analogous situation is found in so-called posterior cisternal arachnoiditis presumably due to extension, to the subarachnoid space, of infection arising in the nose, throat, paranasal sinuses, etc. In such cases, however, there is generalized ventricular dilatation and a cerebellar exploration is usually indicated on the presumptive diagnosis of a posterior fossa tumor. The ultimate diagnosis is made only (1) after a negative exploration (so far as tumor is concerned), (2) the demonstration of a thickened arachnoid membrane with adhesions in and about the fourth ventricle and, most important of all (3) the permanent well-being of the patient after suboccipital craniectomy, as emphasized by Horrax.[24]

V. EPILEPSY

CASE 11.—*Patient with grand mal attacks and status epilepticus. Neurological examination normal. Ventriculogram slightly suggestive of left cerebral tumor. Patient discharged and readmitted two months later with severe fronto-occipital headaches. Clinical signs present. Ventriculogram showed definite evidence of left cerebral tumor. Craniotomy disclosed a glioblastoma of left fronto-temporal region. Radical resection of tumor.*

Dr. M., aged 46 years, a physician, was admitted to the Clinic April 3, 1934, having had pansinusitis several times in the last few years. On admission, his chief complaint was attacks of unconsciousness, of which he had had two in the four months before admission. The first one resulted in status epilepticus, at which time he was thoroughly studied in another hospital but nothing significant was found. He also had suffered periods of amnesia and mental peculiarity, illustrated by the fact that he would start on his morning rounds intending to visit a particular patient in a certain part of the city only to discover himself, in the course of a half-hour or more, talking to a different patient in another part of the city whom he had not intended to visit that day at all. On admission, examination was negative, including normal fundi, plain x-ray films of the skull and visual fields. Ventriculography was performed and normal ventricles were revealed except for possible slight distortion of the left lateral ventricle anteriorly. However, this last finding was too equivocal to warrant anything further as the patient was in such excellent condition. He was readmitted two months later, having had, in the interim, severe fronto-occipital

headaches. Examination showed a questionable right hypesthesia, definite (expressional) right lower facial weakness, and normal fundi. The ventriculogram was repeated and showed definite displacement of the left anterior horn to the right. A left osteoplastic bone flap was turned down and a large glioma was found in the left frontotemporal area, which proved, on histologic examination, to be a glioblastoma. A radical removal of the tumor was carried out and the patient given a year or less of active life.

Follow-up report (ten months after radical removal of tumor): The patient returned to work for several months but, as expected, gradually declined and died on April 15, 1935.

Comment.—This patient represents a group (possibly 15 to 20 per cent of verified tumors) that have normal fundi throughout the course of their illness and only slight ventricular changes in the early stages. Any patient who develops convulsions for the first time after the age of 30 years should be considered as harboring a mass lesion of the brain until it is rigidly excluded. A normal ventriculogram in an adult with convulsions who has a normal cardiovascular system should not terminate the observation of the case. The slightest exacerbation, or the development of new symptoms, demands another ventriculogram and a careful comparison with the first films to exclude a mass lesion. This patient demonstrates the value of a flexible classification as suggested by Cushing; namely (a) tumor suspects, (b) unverified tumors, (c) verified tumors. This particular patient now falls into the last group; whereas, when first studied, he was placed in the suspect class.

CASE 12.—*Post-traumatic epilepsy. Encephalogram normal. (Slight increase in the normal air markings in left occipital area.) Discharged and later readmitted for left cerebral exploration as the right arm became weak in the interim. Post-traumatic adhesions, a depressed inner table, and an enlarged cortical vein disclosed. Postoperative extradural clot evacuated five days later. Uneventful convalescence thereafter.*

Mr. L., aged 33 years, married, a gardener, was first admitted Dec. 5, 1933, complaining of epileptic attacks which were not prevented by phenobarbital. There were no aura. He had had a rather severe head injury in the left parietal region fifteen years previously, at which time he was unconscious for an hour. At the time of admission, he was having an attack every two months with an occasional petit mal seizure. An encephalogram (Fig. 9) showed normal filling of the ventricles, although there was possibly slight increase in size of the left occipital subarachnoid spaces. He was discharged on phenobarbital therapy and, because the attacks continued, he was readmitted on May 24, 1934, for further investigation. By this time the right arm was chiefly involved in the attacks and there appeared, on re-examination of the x-ray films, to be a slight depression of the bone over the left parietal area. A bone flap was turned down over the region in question and post-traumatic adhesions, a depressed inner table of the left posterior parietal region, and a large abnormal cortical vein were disclosed. The adhesions were freed, the depressed bony fragment removed, and the cortical vein ligated. The immediate recovery was excellent, but five days later he showed signs of a left (postoperative) clot as demonstrated by an aphasia and a right-sided paresis, the patient being right-handed. This was removed the same day by reflecting the original bone flap and,

thereafter, the convalescence was uneventful. He was discharged fifteen days following the first operation, having had no further seizures.

Follow-up reports: (1) December, 1934, a letter from the patient stated that he was slowly regaining his strength. No mention was made concerning further seizures. (2) December, 1938, condition about the same as before operation; having seizures about once per month.

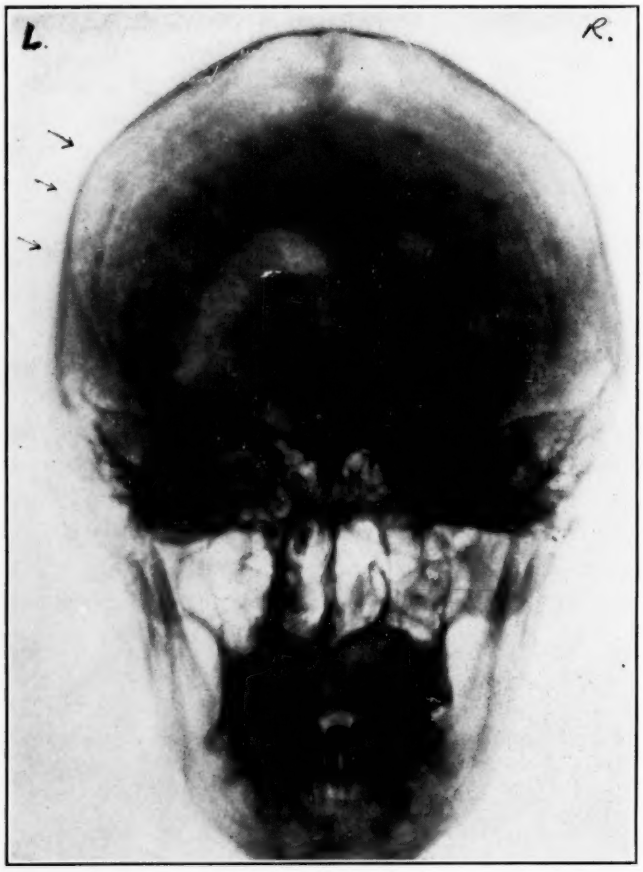


Fig. 9.—Case 12. Encephalogram interpreted as within normal limits except for slight increase in the size of the left occipital subarachnoid spaces (arrows). Operation five months later over the left parietal area (patient had weakness of the right arm) disclosed post-traumatic adhesions, a depressed inner table, and an enlarged cortical vein as causes of the convulsions.

Comment.—Jacksonian epilepsy usually demands exploration of the appropriate motor cortex even if air injection by either route is apparently normal. In this case the definite pathologic changes demonstrated at operation fully warranted exploration, although, as events turned out, the patient was unimproved at last report. All of the findings (with the possible exception of the enlarged cortical vein) were post-traumatic in origin. Occasionally, air injection in post-traumatic cases demonstrates a definite "pulling out" of a ventricle toward the cortical surface. Operation usually demonstrates a cortical scar, often necessitating excision down to the ventricle itself, together with repair

of the accompanying dural defect. The results in such cases are usually excellent. This latter lesion frequently follows compound depressed skull fractures in which the cortex and the dura have been lacerated. In the case described above the lesions were of a somewhat lesser magnitude, but nevertheless quite capable of inducing the disabling epileptic attacks.

DISCUSSION

It is, of course, quite possible that some of the presumptive diagnoses mentioned above may have to be modified in the light of future developments in individual cases. This is true, of necessity, just as it is in any list, for example, of verified intracranial tumors in which a certain proportion of the cases would be temporarily listed as unverified brain tumors or even as brain tumor suspects. One must have, however, a working classification in order that patients may be properly managed when first seen and examined.

Although none of the psychiatric cases described in this paper (Cases 1, 2, and 3) have been proved, to date, to have had a tumor, such a lesion is occasionally discovered. An excellent illustration of this is recorded in the paper by Horrax, Yorshis, and Lavine.[25] A woman 43 years of age, formerly of a high degree of intelligence, had been in a mental institution at intervals for many years with a diagnosis of manic-depressive psychosis. Skull plates showed an enormous calcified tumor in or overlying the left cerebral hemisphere. A ventriculogram was done primarily to determine whether the brain was definitely encroached upon or not; this showed a definite shift of the ventricular system toward the right side. A two-stage removal of an intradural cholesteatoma was followed by remarkable mental improvement so that she was discharged from the sanatorium. She never showed any neurological abnormality; the psychiatric features were the only findings. It is suggested, therefore, that it would be a good plan to take at least one lateral x-ray film of the skull in all psychiatric cases when first admitted to mental institutions so that obvious intracranial tumors of this and other types could be detected and eradicated as soon as possible.

As emphasized in the comment on Case 4 and by Horrax[18] in his introduction to a review of three characteristic cases, cerebral vascular disease frequently closely simulates intracranial tumor in many of its clinical manifestations and resort must occasionally be had to air injections to establish the diagnosis. Cerebral vascular lesions are not invariably apoplectic in onset. On the other hand, intracranial tumors may resemble an apoplexy if a hemorrhage occur in the tumor; this develops, however, much less frequently than is usually supposed. Furthermore, all intracranial tumors are not characterized by progressive loss of neurological function for curious intermittent or sta-

tionary symptoms and signs may be seen in tumor cases which closely imitate cerebral thrombosis. Finally, headache, vomiting, vertigo, choked disk, aphasia, hemiplegia, and ataxia may be present in many cases of malignant hypertension as stated by Pepper[26] and will require a ventriculogram to rule out a brain tumor, although the latter lesion is rarely associated with vascular hypertension per se.

Case 7 clearly illustrates the management of intracranial post-traumatic sequelae. First, an encephalogram was done for its diagnostic and therapeutic effects. After temporary relief, the symptoms recurred and a ventriculogram was performed primarily to exclude the presence of a subdural hematoma. As a liquid clot was found, it was drained through the ventriculogram burr opening. A few months later, the patient returned for a subtemporal decompression on the side of the previous clot because of recurrence of headaches. This is an unusual experience as the great majority of subdural hematomas can be cured permanently by evacuation through a small burr opening.[19, 21, 22]

The diagnosis of arachnoiditis should always be made by exclusion. In Case 9 such a condition is almost certainly correct since so high a degree of choked disks, if caused by a tumor or other mass lesion of the brain, would almost surely have caused some distortion or dilatation of the ventricular system. To support this supposition was the large abnormal amount of fluid released at the time of the right subtemporal decompression which was performed, primarily, for relief of the headache and to preserve vision. In most instances, time alone and the continued well-being of the patient are the best criteria for the accuracy of the diagnosis of arachnoiditis, as demonstrated by the follow-up note in this case.

The chief causes of epilepsy, according to Dandy,[27] are (a) congenital, (b) neoplastic, (c) inflammatory, (d) traumatic, (e) vascular, and (f) degenerative brain lesions. Case 11 demonstrates the wisdom of listing all adult patients with convulsions as brain tumor suspects until a tumor ultimately is disproved or verified. Case 12 includes two of the lesions listed above as the causes of epilepsy: traumatic and vascular.

SUMMARY

1. The value of and indications for encephalography are listed following a review of the literature. It might be summarized by stating that, if increased intracranial pressure be clinically demonstrable or even strongly suspected, this procedure is contraindicated. Even the determination of the spinal fluid pressure by ordinary lumbar puncture is somewhat dangerous in such cases. The practice of doing a Queckenstedt test on *all* patients subjected to encephalography or even lumbar puncture, a method still prevalent in certain hospitals, cannot be too strongly condemned as it yields little or no pertinent information

and may do irreparable harm. The Queckenstedt test should be reserved almost entirely for the demonstration of an *intraspinal block* such as is found in spinal cord tumors and fracture-dislocation of the spine.

2. The indications for and uses of ventriculography are also listed. This procedure is indicated in any patient who presents evidence, however slight, of increased intracranial pressure in the absence of definite signs pointing to a localized lesion. One particular reason for utilizing it in these cases is that, if respiratory or other difficulties supervene following a ventriculogram, relief may be obtained by immediate tapping of the ventricles through the original burr openings; whereas, such a procedure is impossible in encephalography unless cranial burr openings are subsequently made. Furthermore, it has been shown conclusively in most neurosurgical clinics that radical operation for the removal of a tumor should follow the ventriculogram without delay. It is true that in many cases (15 to 20 per cent) of intracranial mass lesions, no evidence of increased intracranial pressure is demonstrable either by x-ray or by clinical examination. If such a lesion be suspected, it is, of course, better to utilize only ventriculography for the localization of the lesion.

3. Five groups of cases are presented to illustrate the value of encephalography or/and ventriculography in determining the necessity for major operation in borderline neurosurgical cases. Representative examples of each group are outlined, the course of the illness in each case is followed, and it is emphasized that, even with an air study, the ultimate diagnosis is not always clear at the time of any single hospitalization period. On the other hand, these relatively minor surgical procedures are often of the greatest aid in deciding upon the immediate disposition of the individual case.

4. It is suggested that, if the above separate indications for encephalography and ventriculography be followed universally, the mortality of 1.2 per cent for the former and of 8.2 per cent for the latter procedure should be still further reduced.

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POSTOPERATIVE MYXEDEMA

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ALTHOUGH there is a great deal in the literature concerning the association of chronic thyroiditis in the form of Hashimoto's and Riedel's strumitis with the occurrence of postoperative myxedema, the literature dealing with the histology of the thyroid gland in those cases in which postoperative myxedema develops is scanty. Smith, Clute, and Strieder reported a series of 100 cases of thyroidectomy, in which series postoperative myxedema developed in fifteen cases, and the authors were impressed with the presence of large acidophilic cells in those cases in which myxedema occurred. They felt that the high incidence of myxedema in their series was probably due to the removal of larger amounts of tissue and to the administration of iodine after thyroidectomy. They found no very close correlation, but a somewhat suggestive parallel, between the degree of strumitis and the incidence of myxedema. McClure and McGraw felt that the amount of thyroid tissue left at operation is the principal factor which determines a normal, recurrent, or hypothyroid state after thyroidectomy. Conklin agreed with McClure and McGraw and stated further that in cases of thyroiditis a large amount of thyroid tissue should be left at the time of operation. He also made the point that, in operations in which a great deal of suturing is required or those which are followed by prolonged drainage or infection, postoperative myxedema is most likely to occur. Jackson contended that in the majority of cases of postoperative myxedema, if not in all, the condition develops because of thyroiditis, which destroys the remnant of the gland left at the time of operation.

The presence of collections of lymphocytes and germinal centers within the thyroid gland of patients with Graves' disease is generally accepted and these collections are said also to occur in normal thyroid glands (Jaffe). The exact significance of these lymphocytes is a moot question, however. Warthin included these in the syndrome of what he called the "Graves constitution," associated with an enlarged thymus and generalized lymphatic hyperplasia. Jaffe considered them secondary phenomena that can be linked to degeneration, involution, hypoplasia, or functional disturbance of the gland. Hellwig expressed the opinion that the collections of lymphocytes in exophthalmic goiter are a local response to hyperplasia and hypersecretion of the thyroid itself. None of these workers associated the presence of considerable numbers of lymphocytes in the thyroid gland at the time of operation with the development of postoperative myxedema.

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Boothby and Plummer stated that there is no clear line of demarcation between the degree of fibrosis and lymphocytic infiltration that can be definitely designated as thyroiditis and the degree of fibrosis and lymphocytic infiltration that is characteristic of exophthalmic goiter. They expressed the opinion that the incidence of myxedema as a postoperative sequela to exophthalmic goiter apparently is roughly proportional to the incidence and degree of chronic thyroiditis. On the other hand, they stated that myxedema sometimes occurs even when no recognizable chronic thyroiditis was present in the tissue removed. Pemberton (Brenizer) stated that in about 10 per cent of all cases of exophthalmic goiter histologic study shows a picture of round-cell infiltration and fibrosis in a degree sufficient to warrant a diagnosis of thyroiditis. In most instances, he said, it is of a mild degree, but not infrequently it is marked and in 0.5 per cent of cases it is very marked. Myxedema invariably develops in these cases, he stated. Broders expressed the opinion that the collections of lymphocytes within the thyroid glands of patients suffering with exophthalmic goiter are a reaction to something within the gland itself, probably thyroxin, or, in other words, that these cells are an attempt by nature to control the thyrotoxicosis.

In this study the term thyroiditis is used to denote collections of lymphocytes within the thyroid gland in sufficient quantities to be an outstanding feature of the histologic picture. An attempt will be made to show the association of their presence with the development of postoperative myxedema.

The material in this paper is based on the histologic findings in the thyroid glands of 238 patients in whom clinical myxedema developed after thyroidectomy. It includes 207 cases of exophthalmic goiter, 19 cases of adenomatous goiter without hyperthyroidism, 1 case of adenomatous goiter with hyperthyroidism, 4 cases of carcinoma of the thyroid gland, and 7 cases in which the thyroiditis was so marked that the classification of the parenchyma was not otherwise apparent. To demonstrate the occurrence rate of postoperative myxedema, all patients who were operated upon in the years 1925 to 1934, inclusive, and who developed postoperative myxedema as late as Jan. 1, 1938, are included in Table I.

Of the 238 cases in the total group, 170 cases (71 per cent) showed a definite amount of thyroiditis. Of the cases of exophthalmic goiter, 72 per cent of the patients had definite thyroiditis at the time of operation. In the group of adenomatous goiters without hyperthyroidism, 66 per cent of the patients showed thyroiditis. The 1 patient with adenomatous goiter with hyperthyroidism who developed myxedema after operation showed no evidence of thyroiditis. Thyroiditis was present in 2 of the 4 cases of carcinoma of the thyroid.

The average interval which elapsed from the time of thyroidectomy until the patient returned to the Mayo Clinic with myxedema, in the group of 68 cases in which thyroiditis was not present, was 18.4 months. In all cases in which thyroiditis was present, the average interval was

TABLE I

RATE OF OCCURRENCE OF POSTOPERATIVE MYXEDEMA (1925 TO 1934, INCLUSIVE)

DIAGNOSIS	NUMBER OF CASES	DEFINITE THYROIDITIS PRESENT (PER CENT)	RATE OF OCCURRENCE OF POSTOPERATIVE MYXEDEMA (PER CENT)
Exophthalmic goiter	161	72	2.1
Adenomatous goiter with hyperthyroidism	1	0	0.06
Adenomatous goiter without hyperthyroidism	12	66	0.3

14.1 months. These cases were divided into groups according to the severity of the thyroiditis at the time of operation, and Table II was obtained. Although the number of cases of severe thyroiditis is small, there seems to be a relationship between the amount of thyroiditis present and the interval elapsing before the patient returned to the Mayo Clinic.

TABLE II

SEVERITY OF THYROIDITIS	NUMBER OF CASES	INTERVAL BETWEEN OPERATION AND PATIENTS' RETURN WITH MYXEDEMA (MO.)
None	68	18.4
Moderate	154	14.7
Marked	13	9.4
Complete destruction of parenchyma	3	4.6

This interval is taken as a basis in this instance, because in a great many cases the onset of symptoms of myxedema was so gradual and insidious that the patient was unable to give any definite time of onset of the symptoms of hypothyroidism.

At the time of operation, each surgeon estimates the amount of thyroid tissue remaining on either side of the trachea in terms of a simple fraction of a normal-sized thyroid lobe. Consideration of these estimations of the amount of thyroid tissue left at the time of operation showed that in cases in which appreciable thyroiditis was not present an average of 0.27 of a normal-sized lobe was left on either side. When definite thyroiditis was present, an average of 0.31 of a normal-sized lobe was left bilaterally. When the thyroiditis was moderate in severity, the amount left was 0.3 of a normal-sized lobe; when the thyroiditis was severe, 0.35 was left, and in extreme thyroiditis, the estimated amount left was 0.36 of a normal-sized lobe on either side. Thus, in this series it is seen that in the cases without appreciable thyroiditis in which postoperative myxedema developed, more tissue was removed, as an average, than in those in which thyroiditis was present.

Another series of 100 cases of exophthalmic goiter was studied histologically and it was found that in only 28 per cent of the cases was there an appreciable amount of thyroiditis present. This contrasts rather

sharply with the incidence of thyroiditis in this series (71 per cent). In this smaller series there was a 2 per cent incidence of postoperative myxedema. Marked thyroiditis was present in both of these cases at the time of operation.

The suggestion that exhaustion may be a causative factor in the production of nonspecific thyroiditis is not borne out by the duration of the symptoms of thyrotoxicosis before operation in this series of cases. In those cases in which no appreciable thyroiditis was present at the time of operation, the average duration of the disease was 24.5 months, while in those cases in which thyroiditis was present, the average duration of the disease was 20.2 months. This finding, however, does not concur with that of Magee, who, in a much larger series of cases of thyroiditis, found that patients with exophthalmic goiter and thyroiditis are hyperthyroid for a longer period before coming for consultation than patients with exophthalmic goiter without thyroiditis. In regard to the duration of preoperative administration of iodine, in those cases without thyroiditis the average period of administration of Lugol's solution before operation was 12.6 days, while in cases with thyroiditis the average was 18.2 days.

That clinical postoperative myxedema is not an irreversible state is demonstrated by two cases in which there occurred recurrent symptoms of exophthalmic goiter, in each case, two years after the patient had been found to have clinical myxedema. In one case, marked thyroiditis was present at the time of operation previous to the onset of myxedema, while in the other, only a few lymphocytes were present. Similar cases have been reported by Haines and by Pemberton. In two other cases there had been present definite clinical myxedema previous to the onset of the symptoms of hyperthyroidism for which operation was performed. In one of these cases there was an adenomatous goiter with hyperthyroidism and at the time of operation definite thyroiditis was present. In the other, a hypertrophic parenchymatous thyroid, no thyroiditis was demonstrated.

In computing the average basal metabolic rate of patients before preoperative administration of iodine had been started, it was found that in cases in which there was no appreciable thyroiditis present the original basal metabolic rate was +45.3. In those cases in which there was appreciable thyroiditis the average basal metabolic rate was +37.9. On subdividing the cases in which there was thyroiditis, it was found that in cases of moderate severity the basal metabolic rate was +42.1; in cases of severe thyroiditis the rate was +37.8, and in cases of extreme thyroiditis the rate was +8.8.

In cases in which thyroiditis was found, the operative wounds drained an average of 2.5 days longer than in those cases in which there was no demonstrable thyroiditis.

In this series the incidence of postoperative myxedema was in a ratio of 1.8 in women to 1 in men. In all cases the incidence of goiter is

usually much higher in women. At the Mayo Clinic the ratio was 2.8 in women to 1 in men in the years 1937 and 1938.

In this series the average age of patients at the time of thyroidectomy was 41.5 years. In those cases in which there was no demonstrable thyroiditis at the time of operation, the average age was 43.9 years, and in those in which thyroiditis was present, the average age was 40.5 years.

SUMMARY AND CONCLUSIONS

In this series an average rate of occurrence of postoperative myxedema in over 15,000 thyroidectomies was found to be 1.2 per cent. Postoperative myxedema is much more frequent in cases of exophthalmic goiter than in those of adenomatous goiter.

Definite thyroiditis was found in 71 per cent of the cases in which thyroidectomy was performed and in which myxedema developed later.

In those cases of postoperative myxedema in which appreciable thyroiditis was not present, the estimated amount of glandular tissue left at the time of operation was found to be approximately 0.27 of a normal lobe on either side, while in cases of thyroiditis the amount left was approximately 0.31 of a normal lobe on either side.

In this series the interval which elapsed between the time of operation and the return of the patient with postoperative myxedema varies inversely, as does the amount of thyroiditis present at the time of operation.

In this series the average basal metabolic rates of patients before the preoperative administration of iodine varies inversely, as does the amount of thyroiditis present at the time of operation.

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A MIXED TUMOR (CARCINOSARCOMA) OF THE BREAST*

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CARCINOSARCOMAS of the breast, although they have been reported only in limited number, have aroused particular concern because of the difficulties involved in their classification. Used in its broad sense, the term, carcinosarcoma, is indefinite, and the question whether these neoplasms are carcinomas, sarcomas, or both is often left unanswered. A variety of names, in addition to carcinosarcoma, have been suggested for this dual tumor, and some of them take the descriptive portion of the combined term from the portion of the malignant lesion present first.

In regard to the etiology of these combined tumors, certain experimental work may help to illuminate the situation. Ehrlich and Apolant found that, while they were transplanting carcinoma of the breast in mice, a different histologic picture suddenly appeared in the tenth generation, for a mixed tumor containing malignant epithelial and connective tissue elements was present. It is of further interest, perhaps, to note that the carcinomatous element had almost completely disappeared by the fourteenth generation. Russell also reported that during the continued propagation of a hemorrhagic adenocarcinoma of the mamma of a mouse, a gradual change in character of the stroma from normal connective tissue cells to malignant cells took place. About fifty-five days was the usual length of time required for this transition, once the phenomenon had been observed in this series. The sarcomatous change having been initiated, it tended toward elimination of the carcinomatous structure and the eventual production of pure sarcoma. Nicholson reported an isolated instance of the development of a small carcinoma in association with a transplanted sarcoma in the rat. He concluded that the observation is a rare one and not previously observed.

From the evidence in experimental work and from a careful review of published cases, it is apparent that the conception of the histogenesis of these tumors is somewhat varied. However, certain possibilities concerning their origin may be postulated:

1. That they spring from one original cell and therefore must belong to the true mixed tumors or teratomas. The cases of Harbitz, Hedrén,

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Wehner, Kunsemüller, and Biebl perhaps belong to this group. Meyer classified this group as "combination tumors."

2. That although the two components are of different origin, one was responsible for the appearance of the second part of the dual tumor. This possibility includes, therefore, the presence of a carcinoma first and the subsequent appearance of a sarcoma, and the reverse situation, with the sarcoma primary and the carcinoma appearing later. These are the "composition tumors" of Meyer. The experimental work of Ehrlich and Apolant and of Nicholson would tend to offer some evidence that this situation may occur. Ehrlich and Apolant advanced two suggestions to account for the appearance of sarcoma in their transplanted carcinoma. A change in the chemical metabolism of the carcinomatous cells may have occurred and this product may have incited the growth of the sarcoma. The second suggestion was that connective tissue elements had been also continuously transplanted and that because of this process they had finally become malignant. It has been shown, however, that the latter suggestion is erroneous, since transplanted connective tissue will degenerate, and the carcinoma derives its new stroma from the host.

Dorsch, Takano, and Kreibig (Case 2) have reported cases in which the carcinoma was thought to have appeared first with the subsequent production of a sarcoma. Kreibig's patient had had an adenocarcinoma of the breast removed one and one-fourth years before the second operation. At the latter time, a recurrent lesion composed of adenocarcinoma and spindle-cell sarcoma with giant cells was removed.

The cases of Kerbirion and Danel, of Coenen, of Wilensky, and of Kreibig (Case 1) fall into the other category, in which the sarcoma seemed to be primary. It is of interest to note that occasionally, as in Coenen's case, a fibroadenoma had existed for some time with sarcomatous development in this benign tumor. Stimulation of the epithelial cells by the sarcomatous focus may cause a second malignant deviation in the fibroadenoma.

3. That the dual tumor arose from different components simultaneously, perhaps uniting to various degrees. This group comprises Meyer's collision tumors. Schlagenhaufer, Kettle, and Curphey have reported cases within this group. Owing to the anatomic relationship in the breast where the two neoplasms were entirely separate, Curphey justified his conclusion that two entirely different malignant lesions were present and arose independently.

The malignant connective tissue elements which may be found in these complex tumors include cartilage, bone, and myxomatous tissue. Many show numbers of giant cells upon microscopic examination. Metastasis of one or the other or both components to the regional lymph nodes has also been noted.

Pasternack and Wirth have reported details of an interesting malignant lesion to which they have applied the name, adenoma acanthoma sarcomatodes. Portions of adenocarcinoma, epidermoid carcinoma with pearl formation, and sarcoma were found upon microscopic study. Pasternack and Wirth concluded that the sarcomatous process was secondary to the acanthoma.

The gross anatomic picture of these combined tumors is multiplex. They may resemble pure sarcoma in one portion and in an adjoining portion look like carcinoma. The zone between them reveals a mixed type of growth. Because of the small number of cases which have been reported, it is without value to ascribe characteristics or peculiarities to this group of neoplasms.

A number of terms have been used to designate these new growths of the breast, and in some the terminology has been derived from the etiologic conception of the author.

The term carcinosarcomatodes has been employed to designate that group in which the epithelial portion of the malignant lesion seemed to have been present first. The tumor arising through the opposite process would thus be called a sarcocarcinomatodes.

Carcinosarcoma, employed by many authors as an all-inclusive term, was used by Wilensky to designate a sarcoma in which carcinoma subsequently developed. If the latter had been the first malignant lesion thought to have been present and a sarcoma had developed later, a sarcocarcinoma would have been present. Fischer-Wasels suggested that carcinosarcoma is a misnomer inasmuch as the malignant epithelial and connective tissue elements in this instance must necessarily arise from one cell.

The demand has been made that the term, carcinosarcoma, if used in its proper sense, be reserved for those neoplasms in which both the carcinoma and sarcoma arose from a common tumor cell. These cells must possess extraordinary lability because of their embryonic failure to differentiate. It would seem with such complex tumors, in which the appearance of either of the components could not be ascribed to the other which was present previously, that they could be more reasonably considered as mixed growths or teratomas.

Carcinomasarcomatoides has been used as a name for a mixed tumor of carcinomatous parenchyma and sarcomatous stroma. No hint as to origin is given in the term.

The term "carcinoma and sarcoma" has been employed where two separate tumors have existed in the breast. There may be little or no anatomic connection between them.

Because of this confusion in nomenclature, it would be much better, depending upon the author's conception of the tumor that he is describing, to designate these tumors as: (1) Mixed growths or malig-

nant teratomas; (2) carcinoma with secondary sarcoma; (3) sarcoma with secondary carcinoma; (4) carcinoma and sarcoma; this would indicate that two entirely separate tumors were present.

REPORT OF CASE

A neoplasm of this dual type was recently studied at the Mayo Clinic. A 50-year-old white married woman reported that for three weeks she had noticed a lump in her left breast. "Twinges" of pain had been present, but she had not noted other symptoms. The tumor had not increased in size and she had not lost weight.

The patient was obese. In her left breast a firm, freely movable, discrete, nontender nodule was found in the upper outer quadrant. There was no change in the skin overlying the tumor, the nipple was not retracted, and the axillary lymph nodes were not enlarged. The heart, lungs, and blood pressure were considered normal. A ventral hernia and some hemorrhoids were also found upon physical examination. The results of routine laboratory examinations of the blood and a roentgenogram of the chest were reported to be normal.

The tumor was removed as a whole, and, after immediate microscopic sections were studied, a radical amputation of the breast was performed. An uncomplicated convalescence was enjoyed and one course of radiotherapy was administered upon the patient's discharge from the hospital. After being advised to have a second course in one month, she was dismissed.

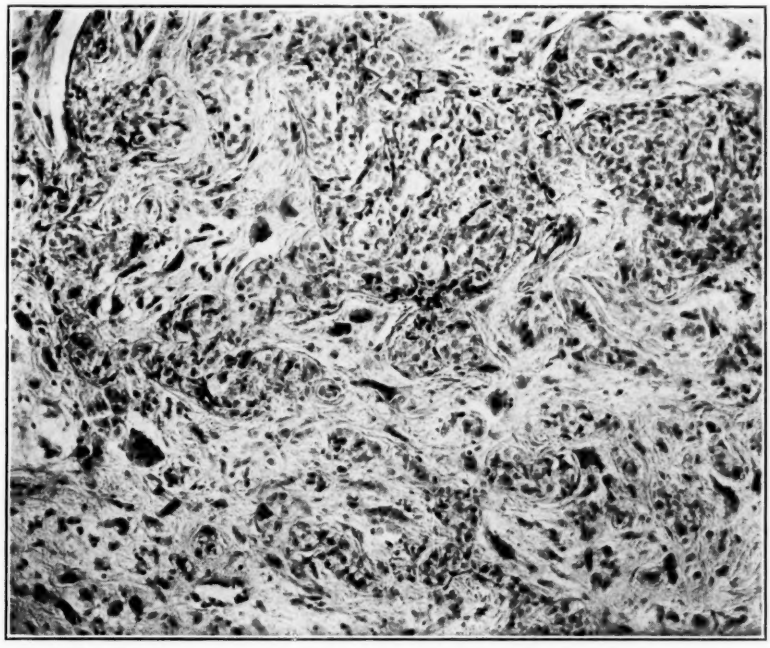

Fig. 1.—Foci of adenocarcinoma in a stroma of sarcoma (×250).

Microscopic study of the removed tumor, which measured 2 by 2 cm., revealed that two types of malignant change were present. Under low power, the outstanding character of the section was the presence of many huge tumor giant cells (Fig. 1). These contained many mitotic figures, both normal and abnormal. The cells were scattered about in a loose stroma which was richly supplied with thin-walled blood vessels. In one portion of the slide, the appearance was that of solid cords of malignant cells arranged in formations suggestive of adenocarcinoma (Fig. 2).

Under the oil immersion lens, the carcinomatous portion was seen to consist of large pale malignant cells with dark nuclei, pale cytoplasm, and definite intracellular boundaries. No definite acini were seen, which was in keeping with the high degree of malignancy.

The sarcomatous portions were composed of huge cells with the general characteristics of the spindle-cell type. Many giant cells of the uni- and multinucleated type

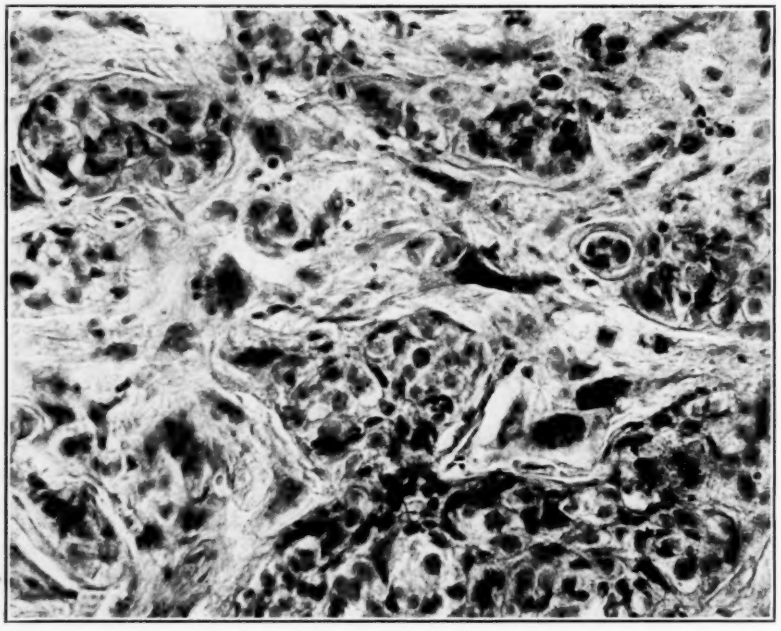

Fig. 2.—Enlargement of Fig. 1 (×215).

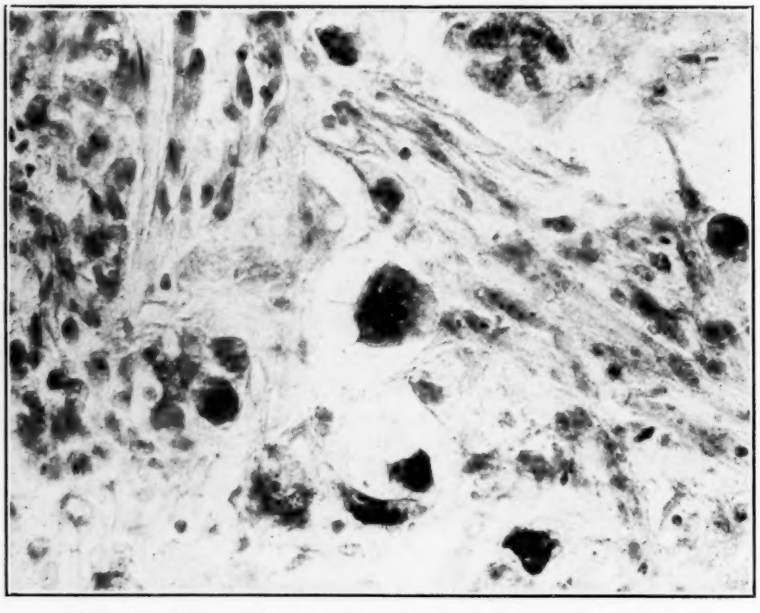

Fig. 3.—Huge mitotic figure of sarcomatous cell (×100).

were present. These were nearly all very malignant in appearance, with huge nucleoli and mitotic figures, the latter assuming varied and bizarre shapes (Fig. 3). The stroma was loose and contained scattered red blood cells, polymorphonuclear leucocytes, and lymphocytes.

The two malignant lesions intermingled, with the sarcomatous cells between the cords of adenocarcinoma. The former were present in greater abundance. Involvement of the axillary lymph nodes by either malignant lesion was not present.

Seven and one-half months after her first admission, this patient was re-examined and no indication of a recurrence could be found. A roentgenogram of her chest was again reported to be normal.

Because of the brief history, the small size of the tumor, the intermingled type of growth, and the fact that neither one of the constituents could be demonstrated to have been present first, this tumor perhaps should be placed in the mixed tumor class.

SUMMARY

The etiology of these dual tumors of the breast is briefly discussed. A discussion of the terminology of the "carcinosarcoma" group of neoplasms is included. A mixed growth of carcinoma and sarcoma is reported.

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FIBROSARCOMA OF THE MAMMARY GLAND*

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"PURE" fibrosarcomas or spindle-cell sarcomas are being found to be more infrequent since it is being realized that the great majority of the sarcomas of the breast have their origin in adenofibromas and are therefore more correctly termed adenofibrosarcoma. Ewing wrote: "When one excludes from the group of mammary sarcomas, the adenosarcomas, the malignant forms of mixed tumor containing cartilage, bone, mucoid or fat tissue and certain malignant round, spindle- and giant-cell alveolar pseudo-sarcomas, which are really atypical carcinomas, there is little remaining of a once formidable group of neoplasms."

The incidence of fibrosarcoma of the breast as reported by several authors has varied considerably, as shown in Table I.

TABLE I

INCIDENCE OF FIBROSARCOMA OF THE BREAST

AUTHOR	YEAR	TOTAL CASES SARCOMA	FIBROSARCOMA	
			NO.	PER CENT
Gross	1887	156		68
Gebele	1901	34	11	32
Finsterer	1907	40	10	25
Geist and Wilensky	1915	22	5	23
		435*	136	31
Fox	1934	60	42	70

*Total collected cases.

It is impossible to compare the statistics in this study with the ones cited, inasmuch as changing pathologic conceptions have sharpened the criteria for diagnosis of these tumors. Grossly, the true sarcomas of the breast have a sameness of appearance in the early stages of their development. The majority are rather well encapsulated, round, irregular, or slightly lobulated, and lie in or next to the glandular structure. At an early stage they are not attached to the skin or the deep tissues, and, consequently, can be rather easily "shelled out" in many instances. Pure sarcoma reaches a huge size only infrequently, in distinct contrast to the malignant lesions which originate in the fibroepithelial neoplasms. On cross section, the new growth varies

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from a gray-white to a gray-red, is of moderately firm consistency, and is usually well demarcated from the breast tissue, perhaps being surrounded by a layer of atrophic ducts and acini.

On microscopic study (Figs. 1 and 2), numbers of fusiform cells are seen lying in close apposition and forming strands that run in different directions, frequently interlacing. Cut in transverse section, these spindle-cell elements are small and round and possess a nucleus which almost fills the cell body. On longitudinal view, the nucleus is relatively large and ovoid and has a well-defined network of chromatin. Mitotic figures are present in varied amount, depending upon the grade of malignancy, while blood vessels may be relatively frequent.

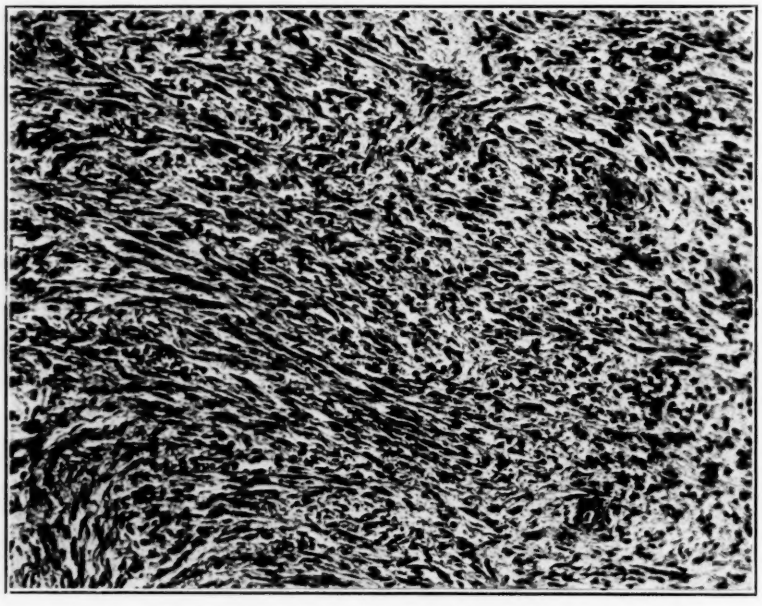

Fig. 1.—Pure fibrosarcoma of the mammary gland (×150).

The regular arrangement of the neoplastic cellular elements about the blood vessels in some of these tumors has caused a few of the earlier authors to err and consider them to be angiosarcoma or perithelioma. Numerous giant cells, which may be either of the tumor or foreign-body type, occasionally are found in these fibrosarcomas. A small amount of fibrillated matrix is found between the cells.

In the years 1911 to 1937 inclusive, nine patients with fibrosarcoma of the mammary gland have been seen at the Mayo Clinic. This number stands in sharp contrast to the twenty-four patients with adenofibrosarcoma which had its origin in adenofibroma. Five patients with fibrosarcoma were seen before being subjected to operative procedure elsewhere. All of these patients were women ranging in age from 44 to 69 years, the average being 49.8 years. Two of these women had noted a mass in the breast for long periods before coming to the

TABLE II

PATIENTS SUFFERING FROM FIBROSARCOMA OF THE MAMMARY GLAND ON WHOM OPERATIVE PROCEDURES HAD NOT BEEN PERFORMED BEFORE THEY CAME TO THE MAYO CLINIC

YEARS WELL	PATHOLOGIC GRADE OF LESION	END RESULT
17	I*	Death from hypertension
Not traced	II*	–
Not traced	II†	–
–	II	Death, postoperative pulmonary embolus
4	IV	Well at present

*Myxomatous change present.
†Tumor giant cells present.

Clinic, while rapid growth of the tumor was noted in these and an additional patient. Three complained of pain in the mammary gland. Radiographs of the chest were normal in the four cases studied. The pathologic grade of the lesion and the end results are shown in Table II. The regional lymph nodes were not involved in any of the cases.

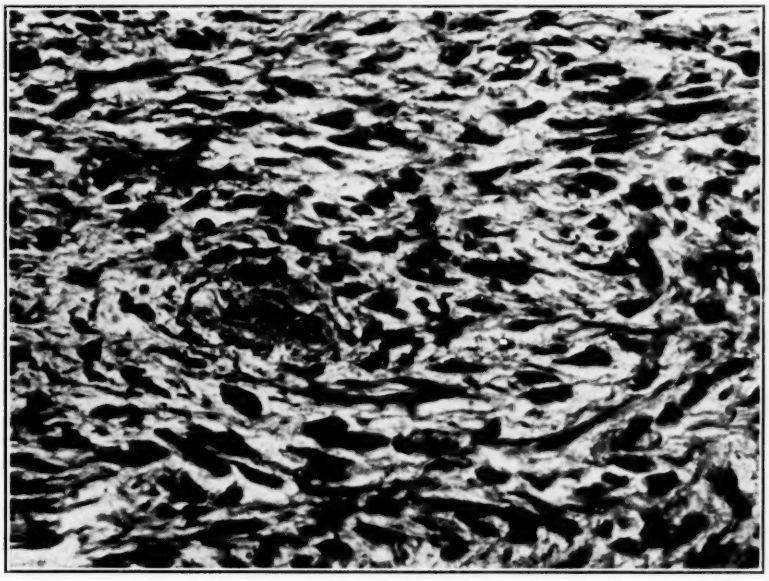

Fig. 2.—Enlargement of Fig. 1. Note spindle shape of cellular elements and occasional mitoses (×420).

Four married women, who had had a previous operation for the malignant lesion for which they came to the Clinic, were seen, and ranged from 32 to 57 years of age. It is significant that these women who had a recurrence were, as a whole, much younger than the group aforementioned All were subjected to operation again at the Clinic. The regional lymph nodes were not involved by the malignant process in any of the patients. End results of treatment are shown in Table III.

It is essential to differentiate between pure fibrosarcoma and adenofibrosarcoma as the cause and prognosis of each are widely different.

TABLE III

PATIENTS SUFFERING FROM FIBROSARCOMA OF THE MAMMARY GLAND WHO HAD HAD A PREVIOUS OPERATION BEFORE COMING TO THE MAYO CLINIC

YEARS WELL	PATHOLOGIC GRADE OF LESION	END RESULT
–	IV*	Death from recurrence in 1 yr.
24	I	Well at present
Not traced	I	–
9	IV†	Well at present

*Tumor giant cells present.
†Tumor and foreign-body giant cells present.

In the latter category the epithelial elements have remained active and dilatation of the ducts and acini has resulted in cystic formations of varying size. Usually the history given by a patient with such a neoplasm is that a mass has been present in the breast for a long time, perhaps years, and that it suddenly has increased in size quite rapidly. Such neoplasms are irregular, large, and lobulated and frequently are complicated by hemorrhage, necrosis, and ulceration. From its initiation, the growth has a tendency to be somewhat circumscribed, and, even though it may become large, it still retains this characteristic. In addition it may be freely movable upon the chest wall. The end results of surgical treatment in this group are much better than they are in pure fibrosarcoma. However, a statistical comparison of this group with patients having "pure" fibrosarcoma will not be attempted owing to the small number of the latter.

SUMMARY

Compared to the incidence of adenofibrosarcoma, that of pure fibrosarcoma (spindle-cell sarcoma) is relatively low. The two types must be differentiated for the history is widely different and the prognosis is much better in adenofibrosarcoma.

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PAINFUL DIVIDED NAVICULAR OF THE FOOT
ITS DIAGNOSIS AND TREATMENT

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PAINFUL divided navicular bones of the foot are common enough so that every practitioner will meet with them several times in the course of his career. So rare is the literature on this condition that the anomaly remains practically unknown, and the affection is labeled usually as ankle sprain, fracture of the navicular, or arthritis.

In a review of the roentgenograms of the feet in 200 unselected individuals, divided navicular bones were found in eight people, or in 4 per cent. Every one of these eight gave histories of sprains or fractures of the foot and indicated the site of the divided navicular as the site of pain. Five of the eight came to us, in a general practice, precisely because of the painful feet. In three of the five, previous x-rays had been taken. Two had been interpreted by general practitioners and one by a radiologist as fractures of the navicular.

So little is generally known of the divided navicular because only two references are to be found in the literature, one by Dwight[1] in 1907 and one by Anspach and Wright[2] in 1937. Its adequate treatment has never been described.

The divided navicular bone, or true tibiale externum, as it has been called (Dwight), develops as an ossification center of the navicular, which, instead of uniting normally with the body of the navicular, makes an independent development as an extra ossicle. It really represents the isolated tubercle of the navicular and is not the small sesamoid often seen in the same region and termed tibiale externum (Dwight). The divided navicular is located at the insertion of the tendon of the tibiale posticus muscle and is firmly fixed in position by the tendon.

The diagnosis of painful divided navicular can be safely made on these points:

1. There is an unusual prominence of the mesial portion of the foot produced by the divided navicular. Tenderness is well localized over and just behind the prominence.

2. On the roentgenogram the smooth contour and texture between the navicular and its divided tubercle mark it as a divided navicular rather than a fracture.

3. Fracture is further excluded by the presence of a similar fragment in the other foot. Divided navicular is a bilaterally occurring anomaly.

The treatment is at first conservative, and, depending on the severity of the pain, bed rest with hot applications or the application of a plaster cast may be resorted to. Frequently however these measures

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are inadequate and the pain continues after the cast is removed or motion is resumed. The most adequate treatment and the one resorted to in three of our cases is simple excision of the fragment. The fragment is easily accessible; its removal neither interferes with the function of the tendon in which it is embedded nor are any joint spaces opened. After excision the foot is firmly bandaged and motion contraindicated for ten days. Thereafter the individual may assume his regular duties and does so with an entire absence of pain.

CASE REPORTS

CASE 1.—G. Y., female, 43 years of age, housekeeper, turned her right foot forcibly in stepping from an automobile. There was no external evidence of injury, but the medial ankle and particularly a point just behind the navicular were extremely painful to pressure. A diagnosis of sprained ankle was made and a physician applied strapping. However, after two weeks the foot was still too painful to allow walking and an x-ray was taken which showed what the physician interpreted as a fracture of the navicular. A cast was applied, but after three weeks tenderness was still present, well localized over the supposed fragment which

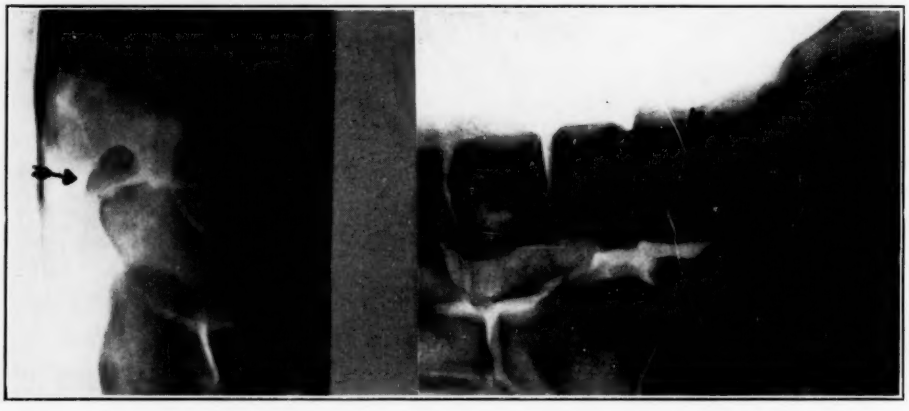

FIG. 1.—Case 1. The divided navicular is clearly shown in both the anteroposterior and lateral views.

failed to show signs of union. On consultation a diagnosis of tibiale externum was made. The small bone was removed in the office. It was found to be very closely united to the navicular in a dense tough fibrous union but definitely separate from it and presenting a flat, faceted surface to the navicular. The foot was immobilized for ten days. Pain immediately disappeared and after ten days walking was begun without pain. After two years no further evidence of pain has been noted.

CASE 2.—J. J., female, aged 10 years, was seen Oct. 29, 1936. In July she had twisted her ankle while running and had a pain over the medial dorsum of the right foot. This was fairly severe but disappeared after a week. In August the pain returned in the same spot, this time without known trauma. This was treated for a time by a physician as a sprain. The pain became worse until the child was unable to walk. Passive motion of the foot was without pain. However, standing on the foot was very painful and there was an area of well-localized tenderness corresponding to what on x-ray was seen to be a true tibiale externum or divided navicular. No redness or swelling was apparent. The sedimentation rate, Schilling, and general physical findings were normal. Conservative treatment, consisting of absolute rest, massage, and diathermy, resulted in no improvement after four weeks.

The small bone was then excised and the pain immediately disappeared and walking was allowed after ten days. The structure and relation of the bone to the navicular were similar to those in Case 1.

CASE 3.—S. J., male, aged 20 years, laborer, turned his left foot while walking over uneven ground and immediately experienced a severe pain over the medial aspect of the foot and ankle. An immediate x-ray of the foot revealed a divided navicular. After five weeks of rest, massage, and passive motion, walking was still impossible and tenderness directly over the small bone was as intense as ever. Again excision quickly relieved pain and restored function.

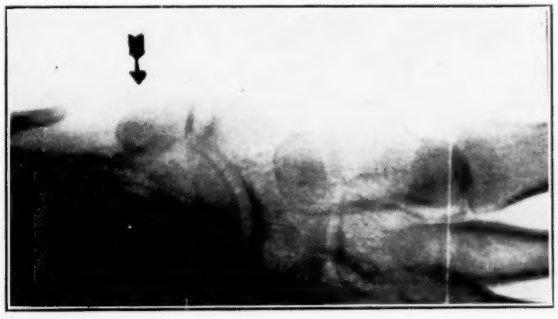

Fig. 2.—Case 2, 10-year-old girl. Divided navicular clearly shown.

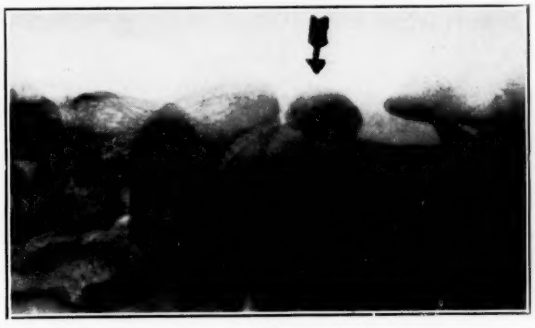

Fig. 3.—Case 3. The divided navicular shows more separation than in the other two cases.

The tibiale externum of each of these three cases was located at the insertion of the tendon of the tibiale posticus muscle and was fixed in position to the navicular by dense tough fibrous tissue. In each case it produced a well-marked prominence on the surface of the foot and this in part may expose it to injury. The adjacent surfaces of the navicular and tibiale externum were smooth and flattened or faceted as though they were surfaces of a joint. Motion in the spaces between them could not be detected under the fluoroscope. The smooth contour and linear margin of density on the opposing surfaces should ward off a diagnosis of fracture of the navicular, and yet this is apparently apt to be made by the inexperienced.

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Editorial

Is There a Hepatorenal Syndrome?

SOME doubt has been expressed concerning the existence of a hepatorenal syndrome. Whether or not there is a direct cause-and-effect relationship between diseases of the liver and kidneys may be open to some question. There can, however, be no question about the existence of a relationship, although the possibility of a single etiologic factor producing the disease in both organs must be admitted. It has been suggested, but not proved, that a soluble substance may be elaborated by damaged liver tissue which has a direct toxic effect upon the kidneys.

In a study of so-called "liver deaths" following operations upon the biliary tract, definite pathologic changes have been found in both liver and kidneys. A retention of nitrogen products and a decrease in the urinary output or a complete suppression of urine have been observed. Albumin, casts, pus, and red cells have appeared in the urine. In some of the cases recorded, a bleeding tendency developed which was evident clinically by bleeding from the mucous membranes. At autopsy blood was found in the serous cavities and hemorrhages were often observed in parenchymatous organs and the mucosa of the alimentary tract.

The results of extensive liver trauma present rather convincing evidence that there is a definite cause-and-effect relationship between the damaged liver and functional and morphologic alterations in the kidneys. There have appeared in the literature a number of case reports which present this evidence.[1] Within a few hours after a severe crushing injury or laceration of the liver, changes in the blood chemistry may rapidly develop with an increase in the nonprotein nitrogen and creatinine. Coincident with these changes there is a decrease in the output of urine with the appearance of albumin, casts, pus, and red blood cells. A study of autopsy specimens of the liver and kidneys shows degenerative changes in both organs. In the kidneys the degeneration is chiefly confined to the epithelium of the convoluted tubules and loops of Henle. These changes occur so rapidly and are so definite that the assumption is reasonable that a toxic substance is elaborated by liver trauma which produces a direct effect upon the kidney epithelium. It must be admitted, however, that the toxic effect may not be direct, but due, as suggested by Boyce and McFetridge,[2] to excessive work placed upon the kidney in an effort to excrete damaged liver products.

Animal experiments have proved the hepatorenal relationship as observed clinically. After severe liver trauma, the same type of changes in the liver and kidneys, blood chemistry, and urine have been described. It must be noted that all animals and all patients receiving traumatic liver injury do not develop evidence of the syndrome. This fact makes an explanation of the syndrome more difficult.

From the evidence which has been presented we may safely conclude that there is a hepatorenal relationship when the liver is damaged by disease or injury, but the explanation of the causative factor or factors and the mechanism of their action upon the liver and kidneys must be determined by future investigation.

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Recent Advances in Surgery

Conducted by Alfred Blalock, M.D.

NEUROLOGICAL CHANGES FOLLOWING SPINAL ANESTHESIA

Review of the Literature and Case Report

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NEUROLOGICAL changes, although infrequent, may follow either general or spinal anesthesia (Woltman[108] and Babcock[9]). Occasionally spinal anesthesia may be falsely accused of causing neurological disturbances until a careful post-mortem examination absolves the anesthetic, as is illustrated by Pemberton's[84] case report.

Lumbar puncture alone rarely has any serious or prolonged sequelae. Purulent meningitis is a potential complication, but it does not occur if aseptic precautions are taken. Reynolds and Wilson[87] reported three cases of aseptic meningitis following diagnostic lumbar puncture, but such a development is so uncommon as to make its cause uncertain. Various authors (Tendler,[99] MacRobert,[71] Heldt,[45] Peluse,[83] Kennedy,[54] Parker,[82] and Nelson[77]) have described the well-recognized headaches, occasionally associated with nausea and vomiting (Parker[82]), which appear from their reports in about 15 to 25 per cent of the cases. These headaches are attributed to the leakage of cerebrospinal fluid (Nelson,[77] Leriche[65]). By the insertion of small pieces of catgut through the hole in the meninges to prevent fluid leakage, Nelson[77] was able to reduce the incidence of headache following lumbar puncture to 4.9 per cent in 102 patients.

Experimental and clinical evidences of neurological changes following spinal anesthesia have been presented following the use of a wide variety of anesthetic agents. That clinical manifestations of such changes are rather infrequent is suggested by the report of Foss and Schwalm[36] of no such complications in 3,000 cases. Pemberton[84] stated in 1933 that he had never seen a serious complication following small doses of the spinal anesthetic agents used in the Mayo Clinic. Lundy[69] also stated that with the use of sterile procaine hydrochloride administered by the usual technique and in "safe" doses they had never noticed any serious changes in the spinal cord. Hyslop[50] gave 0.5 per cent

as the incidence of sequelae in the central nervous system. Frazier[39] discussed definite neurological complications which may follow spinal anesthesia. Because others have experienced such sequelae, these complications are being summarized at this time and a case presented.

The nervous sequelae of spinal anesthesia may be immediate or remote, localized, due to trauma at the site of puncture, or more or less widespread when due to damage from the drug used. Probably there is in every case some toxic reaction produced in nervous tissue by the agents used for spinal anesthesia, but in the majority of cases repair of this damaged tissue is apparently rapid and complete. Occasionally, due to some local or general condition of the patient, recovery is retarded or impeded and therefore we have a few, but widely varied, neurological sequelae which may be temporary or permanent.

CLINICAL SEQUELAE

Headache.—Headache is one of the most frequent complications of either lumbar puncture or spinal anesthesia. Table I presents the num-

TABLE I

HEADACHE FOLLOWING SPINAL ANESTHESIA

AUTHOR	TOTAL CASES	% WITH HEADACHE
Albarron	135	1.5
Beurmer	201	4.9
Chaput	800	0.25
Dax	1,500	4.0
Jones	1,000	0.1
Korte	1,800	0.9
Koster	11,000	5.0
Kronig	1,200	1.0
Legnen	350	1.2
McElligott	500	0.2
Neugebauer	18	83.0
Orkin	45,966	15.5
Steurnagel	320	4.7
Tendler	200	1.0
Woodbridge	1,381	0.5

ber of cases of headache reported by several authors following spinal anesthesia. From these reports, the incidence of headache ranges from 0.1 to 83 per cent. The majority fall within the range of 1 to 25 per cent, comparable to that following simple lumbar puncture.

The onset of the headache may be very delayed,[8] but usually it appears within twenty-four hours after anesthesia. These headaches are often severe. The usual duration is four to seven days, but they may persist as long as one year. Headaches following spinal anesthesia are similar to those following lumbar puncture and are believed to be due, in the large majority of cases, to the loss of cerebrospinal fluid by seepage from the hole left in the dura.[71] Increase in cerebrospinal fluid pressure and meningeal irritation also are possible causes.[5, 83]

Nausea and Vomiting.—Nausea and vomiting, either separately or together, occur not infrequently. Jarman[52] reported an incidence of 0.5 per cent and Garside[41] an incidence of 5 per cent in 357 cases. Thirty-three of Tendler's[99] 200 cases vomited within twenty minutes after injection. Fifteen per cent of Jones'[53] 1,000 cases had nausea or vomiting. Neugebauer[78] had 13 out of 18 cases vomit.

Nausea usually occurs within the first fifteen minutes after the injection of the spinal anesthetic and subsides within the first half-hour. This symptom seems to accompany or follow closely the blood pressure reaction. Nausea and vomiting, in our experience, rarely persist after the action of the anesthetic agent has disappeared. Vomiting may be due to morphine, the operative procedure (traction on the bowel or pressure on the stomach), or even the psychic reaction of the patient, as well as the anesthetic drug.

Respiratory Paralysis or Sudden Death.—Of the immediate sequelae, paralysis of the anterior roots of the phrenic and intercostal nerves and failure of the respiratory center are the most striking. Jarman[52] stated that "sudden collapse" occurred in 0.01 per cent of the cases. Buxton[24] reported 8 cases (6 from the foreign literature) in which sudden respiratory failure occurred soon after the injection. All of these were resuscitated, one after artificial respiration had been administered for five hours. Falk[33] had 3 deaths from respiratory failure before the operation was begun. Several authors report respiratory failure or collapse usually occurring soon after injection, sometimes at the close of the operation and sometimes several hours after operation. Kader (see Violet and Fisher[104]) had 8 instances of respiratory arrest in 1,900 cases. Others reporting early respiratory failure or collapse are: Rapaport,[85] 4 cases; Arnheim and Mage,[7] 1 in 497 cases; Violet and Fisher,[104] 3 in 270 cases; Tendler,[99] 1 in 200 cases. Veal and van Werden[103] report 30 immediate fatalities in 33,811 cases. These deaths occurred in the operating room shortly after the spinal anesthetic was given. Jones[53] reported 6 instances of "collapse" in 1,000 cases. Among these he observed 1 case of respiratory failure at the end of operation with death on the fourth day. Brunn[21] reported 1 sudden death during operation, 1 sudden respiratory death sixteen hours postoperatively (no pathologic findings at post-mortem examination); 1 sudden respiratory death twelve hours postoperatively; and 1 on the ninth postoperative day. The last presented at autopsy very marked arteriosclerosis of the brain and numerous intracerebral softenings. Woodbridge[109] had 1 case with complete respiratory paralysis seventeen minutes after injection. The patient was resuscitated. Bodechtel[16] reported a case of convulsions on the third day following spinal anesthesia with death from respiratory paralysis. A hemorrhage in the left parietal region was found at post mortem. Chaput[23] reported 4 cases in which "syncope" occurred.

We have seen in our clinic 2 cases of convulsions and death in young children following injection of 1 per cent novocain under the scalp for operations upon the brain. The cerebral pathology present makes them unsuitable for comparison with other cases. However, it may be that the patient's sensitivity to novocain alone in any site may be responsible for some of the sudden deaths under spinal anesthesia.

Cranial Nerve Involvement.—Cranial nerve palsies, as postoperative complications, may be seen in patients who have had general or regional as well as intraspinal anesthesia. One case which Woltman[108] cited had a left abducens palsy appearing eleven days after laparotomy under ether anesthesia. This palsy disappeared in seven days. A left third nerve palsy appeared in another patient six days after an appendectomy under gas and ether anesthesia. This patient had at the time a subsiding phlebitis of the left leg.

Cranial nerve involvement may also follow lumbar puncture or spinal anesthesia. Table II presents some of the cranial nerve involvement that has been reported.

Of all the cranial nerves, the sixth is the most frequently paralyzed. Anderson[5] stated that abducens paralysis may occur in from a few minutes to two weeks after intraspinal injection of the drug. It may be accompanied by photophobia and last seven to ten days. Chiene's[24] 30 cases varied in onset from the ninth to the twelfth postoperative day, and the duration was from three weeks to six months. Ashworth's[8] patient completely recovered in eight weeks. One of Hughes'[49] 2 cases lasted seven weeks.

In Rollett and Berard's[88] cases the paralysis lasted one week to four months. They believed these palsies were due to a mild meningitic reaction. Franke[37] mentioned Adams'[2] explanation of abducens paralysis, which also has been reported following lumbar puncture alone (Gabrieljan[40]), as being due to hemorrhage as a result of alternations in the intracranial pressure. Woltman[108] stated that the cause is unknown.

Smith[92] mentioned mild meningeal reactions after spinal anesthesia, at times associated with an ocular palsy. Nystagmus is a common transient phenomenon according to Pallestrini.[81] DeCourcy[29] had a case with nystagmus appearing ten days after a spinal anesthesia and lasting several weeks. Kennedy[54] had one transient diplopia in 470 cases. Disseminated sclerosis was present preoperatively in this patient.

To summarize the data obtained from twenty-five authors (Table II) who have reported extraocular muscle paralyses, it is apparent that this complication may appear in a few minutes to a few weeks following the anesthesia and last for one week to several months.

Hemiplegia.—Hemiplegia has occurred postoperatively after both spinal and general anesthesia and a wide variety of operative procedures. It is difficult to say in any case in which it developed after spinal anesthesia that it was definitely due to the anesthetic agent. Woltman[108]

TABLE II

CRANIAL NERVE INVOLVEMENT FOLLOWING SPINAL ANESTHESIA
(VARIOUS DRUGS USED)

AUTHOR	TOTAL CASES	6TH	2ND	3RD	4TH	7TH	8TH	12TH	3RD, 4TH AND 6TH	MIXED
Adam		1								
Adams									1	
Angelescu and Tzovaru										1 (8th and 12th)
Ashworth	650	1					2			
Babcock	12,000	5								
Becker										1 (3rd and 6th)
Blatt review of literature		78	2	1	4	2				7
Bodechtel		1								
Borchardt		1								
Brenner-Goldschwend	2,600	6								
Chiene	12,000	30								
Dax		6								
Deetz		1								
Fawcett	2,000								5	
Franz		3								
Gabrieljan	4,000	1								
Gottschalk		1								
Hughes	500	2								
Jacqueau			1							
Kirschner	4,000	3								
Knobloch										1 (6th and 5th)
Korte	1,800			1						
Landow		1								
Lindemulder		1								
Loeser		2								
MacLachlan										1 (ocular)
Orkin	45,966	0.7%								
Roeder					4					
Schepelmann		1								
Sellheim	1,000								9	
Sonnenberg	1,181	3				1		1		1 (5th and 6th)
Strauss										32
Violet and Fisher	Collected								44	12
Woltman		1								
Backer-Grändahl		2								
Nygaard	1,198						1			1 (6th and 7th)

mentions thrombosis, embolism, and unknown causes in discussing the etiology of such hemiplegias. Seven reported cases following spinal anesthesia appear in Table III.

Paraplegia.—Mennell[74] stated that neurologists recognized an entity, "stovain tabes." Neugebauer[78] reported one case of paraplegia. In another series where tropococaine was used in amounts higher than 0.05 c.c. of 5 per cent solution, 10 out of 18 cases had paralysis of the legs lasting several hours. Violet and Fisher's[104] 16 cases were from sixteen authors who used four different agents. In the majority of cases recovery was spontaneous in from five days to five months. One of Steuernagel's[96] 3 cases lasted three months, then recovered. The others were transient. In one case eight days postoperatively neurological changes were noted, especially involving the right leg. Hewer's[47] case

TABLE III

NEUROLOGICAL CHANGES WITH VARIOUS SPINAL ANESTHETIC AGENTS

AUTHOR	PERIPHERAL NEURITIS AND RADICULITIS	MYELITIS	ENCEPHALO-MYELITIS	TROPHIC CHANGES	HEMI-PLEGIA	CORTICAL SOFTEN-INGS
Aguglia		1				
Arnheim and Mage		1			3	
Ashworth	1	2				
Babcock	1					
Bedeschi		2				
Bergmann	1					
Brenner-Goldschwend						4
Brock, Bell, and Davison	2	2				
Dassen					1	
Devraigne					1	
Flath		1				
Franke		2				
Goldman				1		
Gottschalk	1					
Hesse	1			1		
Hewer	1					
Hohmeier		1				
Hughes		3				
Jones	1					
Legnen		3				
Lindemulder		1	1			
Loeser	5					
MacLachlan			2			
Marjantschick		1				
Michelson		4				
Müller		2				
Neugebauer		4				
Nonne and Demme		2				
Pugh		1				
Sellheim	1					
Shepelman	1	1				
Silva		1				
Smith		1				
Steuernagel		3				
Stout	4					
Sudeck				1		
Tabanelli	1					
Trantenroth	2					
Urban	1	2				
Waitz		1				
Waters	2					
Woodbridge	12				2	
Nygaard			1			

had incontinence and one leg paralyzed and analgesic, the other leg somewhat affected. Nine months later laminectomy showed a fibrous band constricting the lower spinal cord. Improvement followed removal of the band.

Nonne and Demme's[79] case had paralysis of both legs, bowel, and bladder which persisted from the day of operation until death two years later. He had received tutocain spinal anesthesia for a bilateral inguinal herniotomy. Necropsy revealed adhesions between the pia and

the dura mater in the lower part of the spinal canal. There was ascending degeneration of almost all of the posterior columns of the lumbar and sacral cord, but the posterior roots and horns were intact. The brain showed no histopathologic changes. Of Michelson's[75] cases, 2 eventually came to necropsy. Thickened meninges adherent to the spinal cord were found.

Quadriplegia.—Devraigne, Suzor, and Laennec[31] reported a case of quadriplegia. In this case 5 per cent novocain was used. Four days postoperatively the patient developed loss of muscle tone in the legs. On the fifth day a complete flaccid quadriplegia was present. On the eighth postoperative day there was rapid and spontaneous recovery with slight residual impairment of extensor strength in the lower extremities.

Bowel and Bladder Disturbances.—Neugebauer[78] reported 3 cases of temporary anal sphincter paralysis following tropococaine. Waters[106] had 1 such case out of 297 patients. In this case the paralysis lasted twelve days. Beurnier[104] had 1 in 210 cases. Silva[91] saw 1 case with permanent bowel and bladder paralysis after spinal anesthesia for the removal of an inguinal node. Hughes[49] had 3 cases in 500. One had retention for many months, one had loss of bladder power and anal analgesia, and a third was incontinent. Arnheim and Mage[7] had 2 cases out of 497 who had urinary retention. Bedeschi[12] reported paralysis of the anal sphincter in 2 out of 294 cases with amylocaine hydrochloride. One subsided after ten days, the other after thirty-five days. Cystitis and decubitus ulcers developed in the second case.

Neuritis and Sensory Disturbances.—Woodbridge,[109] in a study of 1,381 cases, reported the following: hyperesthesia in 2; numbness in 2; anesthesia of the thigh in 1; and coccygodynia in 1. Paresthesias were reported by Orkin[80] in 0.19 per cent of 45,966 cases; Brock, Bell, and Davison[20] saw 2 cases of cauda equina neuritis. Jones[53] reported 1 case of sciatic pain lasting six months after a spinal anesthesia. Brunning[104] stated that he had several out of 200 cases who had persistent pain in the legs. Waters[106] cited 2 cases out of 297 that had pains in the lower extremities for some time after leaving the hospital.

Sellheim[90] saw 1 instance of radial nerve involvement in 1,000 cases. Lindemulder[66] reported a case of severe pain in the upper extremity. This patient died and changes in the dorsal and lumbar cord were found at necropsy.

Woodbridge[109] had 4 patients with transient foot drop following metycaine spinal anesthesia. Schepelmann[89] had 1 case in which foot drop appeared on the eighth postoperative day and recovered completely in one year. McElligott[73] observed 1 foot drop following 500 scurocaine anesthetics.

Brock, Bell, and Davison[20] saw a case of lumbar radiculitis appearing three weeks after injection of the anesthetic. Babcock[10] had 1 case of violent radiculitis in 12,000 cases. He attributed this complication

to injection of the drug into a nerve root. Anderson[5] stated that radiculitis may develop and last several months, but eventually recovery occurs.

Backache.—Backache, at least in a mild degree, probably occurs more frequently than is reported because of difficulty in evaluating this complaint. Tendler[99] in 200 cases had 1 instance of severe backache lasting one week. Woodbridge[109] reported 3 instances of backache in 1,381 cases and Jarman[52] stated that backache occurred in 0.02 per cent of the cases after spinal anesthesia.

Myelitis.—Smith[92] observed one complete transverse myelitis in the ninth thoracic segment which appeared on the seventeenth postoperative day. Brock, Bell, and Davison[20] and Arnheim and Mage[7] each reported 1 case of transverse myelitis. Franke[37] observed 2 such cases with permanent paralysis. Orkin[80] gave 0.16 per cent as the incidence of myelitis. Nonne and Demme[79] reported a case following the injection of tutocain. See Table III.

Meningitis and Encephalitis.—The occurrence of infection following spinal anesthesia is perhaps the most easily explained of all the complications and can be prevented by aseptic technique. The etiology of

TABLE IV

MENINGITIS FOLLOWING SPINAL ANESTHESIA

AUTHOR	SEPTIC	ASEPTIC	? TYPE
Arnheim and Mage	1	1	
Ashworth	1		
Bodechtel	1		
Brock, Bell, and Davison		3	
Brunn	1		
Campbell	1	1	
Hyslop			1
Orkin	9		
Rehn	1		
Schepelmann			1
Sonnenberg	3		
Violet and Fisher	1		

the "aseptic" meningeal reactions is not clear. Table IV presents a summary of some reported cases. *B. pyocyaneus* was isolated from Arnheim and Mage's case.[7] Orkin[80] reported an incidence of 0.26 per cent of meningitis and encephalitis. He found 9 cases of septic meningitis in 15,000 collected cases. These 9 and the 1 recorded by Arnheim all ended fatally. Campbell[22] reviewed the histories of 2 patients who developed meningitis. One presented at necropsy a monocytic meningitis with a large intraventricular hemorrhage; the other, acute purulent meningitis, intraventricular hemorrhage, and diffuse ganglion cell degeneration in the cerebral cortex. The organism was undetermined in the latter. The first case had preoperatively multiple small furuncles over the body and an acute cystitis. The second had an abscess of the heel. Brock, Bell, and Davison[20] reported 1 case of polioencephalitis;

Lindemulder,[66] 1 case of encephalomyelitis; Ashworth,[8] 1 nonhemolytic streptococcus meningitis beginning twenty-four hours postoperatively; Schepelmann,[89] 1 case of meningitis which expired four days postoperatively; Violet and Fisher,[104] 1 death of suppurative meningitis eight hours postoperatively; Sonnenberg,[93] 3 cases with septicemia and suppurative meningitis; Rehn,[86] 1 death thirty hours postoperatively of suppurative meningitis; and Brunn,[21] 1 purulent meningitis. The last patient had a septic course before the spinal. Bodechtel's[16] case had meningitis with brain hemorrhage. Reynolds[87] reviewed 3 cases of aseptic meningitis following diagnostic lumbar puncture. The patients had fever, stiff neck, and positive Kernig's sign. All recovered.

MISCELLANEOUS COMPLICATIONS

Hadfield[44] reported a death due to *bronchial spasm* and also one due to *increased dyspnea* in an asthmatic patient after spinal anesthesia. Stillwell[97] had a case of *massive pulmonary collapse.*

Obviously, *hysteria, hallucinations,* and *delirium,* as well as the true *psychoses,* are complex in origin and can never be unquestionably attributed to a spinal anesthesia as their simple cause. In fact, Woltman[108] stated that when a truly "postoperative psychosis" develops it almost invariably follows an inhalation anesthesia, usually including ether. He could not find a single case at the Mayo Clinic of true postoperative psychosis following a spinal anesthesia. Woodbridge[109] included 1 case of hysteria in his review. Munchmeyer[104] had 2 instances of "traumatic hysteria" in 1,000 cases. Reznier[104] saw 1 case of paralysis of the extremities and neck with complete recovery in fifteen days, which he attributed to hysteria. Mingozynini[104] reported "hysterical convulsions" for eight months following a spinal anesthesia. Steuernagel[96] had 1 out of 320 patients develop a psychosis. Orkin[80] gave the incidence of psychosis as 1.8 per cent. Brunning[104] reported 2 in 2,000 cases. It is the general belief that persons with any changes of the central nervous system should not be given a spinal anesthetic.

MIXED COMPLICATIONS

Dandois[25] had a patient develop headache and convulsions after cocaine spinal anesthesia and on the ninth postoperative day a complete paraplegia. Delirium and mania then began and lasted one month. The author questioned this being a meningoencephalitis because of an afebrile course.

Bodechtel[16] reported convulsions three days postoperatively, after a novocain spinal anesthesia, with later facial paralysis, respiratory paralysis, and death. Necropsy revealed a cerebral infarct. There was no examination of the spinal cord. One patient died at the end of an operation performed under tropococaine spinal anesthesia and avertin. Necropsy revealed no cause of death, and the spinal cord and brain

were said to have been normal. In another instance where avertin and tropococaine were used, sudden unconsciousness and convulsions developed two days postoperatively. Six days later a paralysis of the left external rectus muscle appeared and the patient died on the sixteenth postoperative day. There were multiple hemorrhages throughout the brain and spinal cord. Bodechtel[16] believes that circulatory changes produced by spinal anesthesia may favor the occurrence of hemorrhage and thrombosis in the central nervous system.

Schepelmann[89] had a patient who was very restless during and after the operation. He became unconscious and remained so for three days and for weeks was irrational and incontinent, with paralyzed sphincter, bladder, and legs. A diagnosis of "myelitis lumbalis" was made. Years later the patient was slightly improved.

Guinard[104] described "syncopes" followed by fever, intense headache, and a meningeal reaction. Ashworth[8] reported an instance of leg pain beginning soon postoperatively and followed one year later with occipital headache. This author also had a case with headache three days postoperatively and later failing eyesight and tingling and numbness of the right leg. He stated that late studies of neurologists showed that 4 of 202 cases after spinal anesthesia had nervous sequelae.

Pemberton[84] discussed a case that developed meningitis following a Mikulicz operation under spinal anesthesia. On the seventh postoperative day manifestations of meningitis appeared, with death on the tenth day. Necropsy revealed acute purulent meningitis limited to the vertex which was probably blood-borne from a small pulmonary abscess which had developed around a small metastatic carcinoma growth. These findings perhaps absolved the spinal anesthetic. He stated that "there is a tendency for the surgeon to attribute to the anesthetic or its mode of administration any unusual complications which cannot readily be accounted for otherwise."

The following case report is made in an effort to add to the records of sequelae that may follow spinal anesthesia. It is necessary, however, to bear in mind the above statement of Pemberton, as we in no way wish to discredit the selective and indicated use of this type of anesthesia.

CASE REPORT

Mrs. V., age 38 years, was a patient who had had a diarrhea of ten to twelve stools daily for six months, a loss of 75 pounds in weight, abdominal cramps, and progressive weakness to the point of inanition. She appeared cachectic and acutely ill. Her blood pressure was 118/58. The cardiovascular system was apparently normal. The lungs were clear. The abdomen on palpation gave a sense of fullness which was neither tympanitic nor ascitic. There was tenderness over the region of the sigmoid and descending colon. The liver was palpable two finger-breadths below the costal margin, smooth and nontender. Her red blood count was 4,450,000; hemoglobin, 65 per cent; and white blood count 18,100, with 76 per cent polymorphonuclear leucocytes, 2 per cent large lymphocytes, and 3 per cent small lymphocytes. The urine contained one plus albumin. The blood Wassermann

and Kahn tests were negative. Her temperature ranged between 100 and 104° F. On proctoscopic examination much creamy mucoid material was obtained, and a large rectovaginal fistula was seen. There were no amoebae in the stools. X-ray studies of the gastrointestinal tract indicated a regional ileitis.

The diarrhea was controlled by medication; but the fever and loss of weight continued in spite of blood transfusions and supportive treatment, so resection of the affected bowel was advised. When the patient was brought to the operating room, she appeared pale and cachectic. She looked 50 years old instead of 38, her actual age. She complained that her "chest was too tight" and her mouth dry. She breathed loudly through her mouth and talked in a rambling fashion. She cooperated well, but she did not seem to realize that she was in an operating room or having an operation. Her skin was dry, her tongue coated, and her breath foul. She was coughing and expectorating thick sputum. A chest examination was negative. Her pulse rate was 112 and blood pressure was 110/70. Spinal anesthesia was used; 140 mg. of novocain crystals dissolved in 5 c.c. spinal fluid were injected in the spinal canal at the third lumbar interspace. A 20-gauge Lundy spinal needle was used. Anesthesia to the fourth dorsal level was obtained. At the end of the operation, the patient felt the last few skin stitches. Her condition was good throughout the procedure, which lasted one hour and twenty minutes. Eighteen inches of ileum were removed, and a lateral anastomosis of the ileum and anterior surface of the cecum was made.

Following this operation the patient seemed to be improving slightly up to the ninth day, when she suddenly had a severe chill and temperature elevation to 103° F. Then her condition gradually became worse in spite of many blood transfusions. On the eighteenth postoperative day she complained of difficulty in breathing. A chest examination at this time showed nothing essentially abnormal, but by the next day she was obviously using the accessory muscles of respiration. A diagnosis of paralysis of the diaphragm was made and verified by fluoroscopic examination. A neurological examination showed, also, a flaccid paralysis of both lower extremities with bilateral positive Babinski reflex. She was placed in a Drinker respirator, but there was no improvement, and on the twenty-eighth postoperative day she expired after vomiting and aspirating the vomitus.

Post Mortem Examination.—The weight of the body was 62 pounds. There was obstruction of the trachea and main bronchi by stomach contents and overexpansion of both lungs. A very early bronchopneumonia was found. The right pulmonary artery was thrombosed. The heart was small and showed fibrous thickening of the mitral valve. The esophagus was small, measuring only 2 cm. in circumference.

The terminal ileum was absent with a side-to-side enterocolostomy. There were regional ulcerative ileitis and colitis with a small perforation in the transverse and descending colon. The portal and splenic veins were thrombosed. Cholelithiasis was found with obstruction of the neck of the gall bladder and dilatation of gall bladder with white bile. There was slight fatty degeneration of the liver. There were a large rectovaginal fistula and two ischiorectal abscesses with fistulas. There were marked vaginitis and cervicitis. The bladder was diffusely inflamed and there was an ascending ureteropyelitis with multiple abscesses in both kidneys. There were multiple phleboliths of the veins of the broad ligament. There were an old thrombus in the right iliac vein and recent thrombosis of the left iliac vein.

The only abnormalities in the central nervous system apparent on gross examination were dilated and engorged vessels in the lepto-meninges over the cerebral hemispheres and in the thalamus, and numerous pin-point hemorrhages in the right mammillary body.

In an individual with such severe and extensive systemic infection one expects to find on microscopic examination marked changes in the appearance of the

ganglion cells in the central nervous system, changes described by Nissl under the heading of acute disease of the nerve cells. The cell body becomes swollen; the fundamental unformed substance of the cell, the hyaloplasm, stains more deeply with basic solutions and this process extends into the axone and dendrites so that the ramifications of these can be followed for greater distances than normally is the case. The nucleus swells, moves toward the periphery of the cell, and the nucleolus enlarges. The glial elements show both progressive and regressive alterations: progressive indicated by cell division and accumulation of glial nuclei around abnormal nerve cells, the process of neuronophagia; regressive indicated by hyperchromatosis of the glial nuclei. These changes were seen in this case spread diffusely throughout the brain. Examination of four areas of the cerebral cortex, of the thalamus, the lenticular nucleus, the small nuclei in the wall of the third ventricle, and both mammillary bodies revealed this acute, nonspecific disease of the nerve cells, which we have attributed to the patient's extensive systemic infection.

In addition the right mammillary body showed hemorrhagic softenings, multiple small areas in which there was complete destruction of all of the cells, and the presence of only vague cell shadows and accumulations of yellow hematoidin pigment. There were a marked proliferation of capillaries and a profuse overgrowth of glia along with acute disease of the nerve cells in those areas of the mammillary body not occupied by the softenings. Bodechtel[16] has described 1 brain in which there were numerous hemorrhagic infarcts in a patient who died on the second postoperative day following an operation under novocain spinal anaesthesia, and Brenner[19] has described 4 autopsies in which softenings of the brain were found following spinal anesthesia. In the case we are reporting the patient's poor general condition and consequent poor circulation were more than adequate to account for the changes found in the right mammillary body without implicating spinal anesthesia. Since the areas of softening here were several weeks old it is a possibility, but in no way a proven fact, that they might have arisen during the period of somewhat poorer circulation at the time of spinal anesthesia and operation.

We come now to the changes seen in the spinal cord and brain stem. Eight different blocks from the cord were studied, and Nissl, fat, Weil, and Spielmeyer stains for myelin, and Marchi stain, hematoxylin and eosin, and Freeman's silver stain for axis cylinders were used. With the Nissl stain most of the nerve cells in the lumbar cord show the so-called retrograde type of degeneration in varying stages of severity, but usually in an advanced stage. The cells are swollen and rounded; their protoplasmic processes seem to have vanished right up to the cell origins; the Nissl bodies in the cytoplasm have largely or completely disappeared, leaving the cell body with a light blue opaque ground glass appearance. The nucleus is eccentric, may produce a humplike protrusion of the cell membrane, or may be completely extruded. In the thoracic cord scattered cells not only in the anterior horns, but also in Clarke's column and in the intermediolateral cell column show these retrograde changes. But in the cervical cord, the medulla, and the pons, except for marked degeneration in the dorsolateral cell column, the majority of the cells appear normal. In the fat stains large globules of orange-staining lipoid are seen to be present in the degenerated cells. In the stains for myelin the anterior and posterior roots in both their intramedullary and extramedullary portions are seen to be either extensively or completely demyelinated. This change is present in all of the sections. In the lumbar portion of the cord and to a less extent in the thoracic and cervical regions there is a zone of peripheral demyelinization extending inward a variable distance toward the center but present to some extent around the entire 360 degrees of the circumference of the cord. In the demyelinated fibers there is some swelling, but there is no increase in sur-

rounding glia, and the involved areas have the moth-eaten appearance seen in subacute combined degeneration of the spinal cord. The Freeman stain shows the axis cylinders to be essentially normal.

HISTOLOGIC STUDIES OF THE EFFECTS OF SPINAL ANESTHETIC AGENTS IN ANIMALS

Koster and Kasman[60] found that retrograde degeneration of ganglion cells in the cord and medulla oblongata is produced in frogs by spinal anesthesia with procaine and that these changes begin to regress in three hours. Twenty-four hours after the injection, the frog's spinal cords are again normal.

Fig. 1.—Nissl stain (×325). Anterior horn cells in lumbar region. Severe retrograde type of degeneration in cell at upper right; milder degree of same type in cell at lower left.

It has been shown in animal experiments by van Lier[102] (1907) that normal dogs given a subarachnoid injection of stovain show retrograde degeneration in the cells of the lower spinal cord, reaching a maximum by six hours and returning almost completely to normal twenty-four hours after the injection. Wossidlo[110] (1908), using stovain, alypin, and novocain in rabbits, came to essentially the same conclusion. Spielmeyer found in one dog and three apes which had a flaccid paresis of the lower extremities following single or repeated stovain spinal anesthesias that there was not only persistent retrograde ganglion cell de-

generation in the anterior horns of the spinal cord but also a demyelinization of the posterior columns and posterior roots, and in one ape and one dog there was a demyelinization around the entire periphery of the cord extending in irregularly toward the center. Klose and Vogt[56] gave dogs and rabbits spinal anesthesia with stovain, novocain, and tropococaine. They found no changes in the ganglion cells from two hours to two days after injection, but subsequently the reaction of degeneration was seen in some of the cells of the anterior and lateral horns of the lumbar and dorsal regions and to a lesser extent in the cervical region.

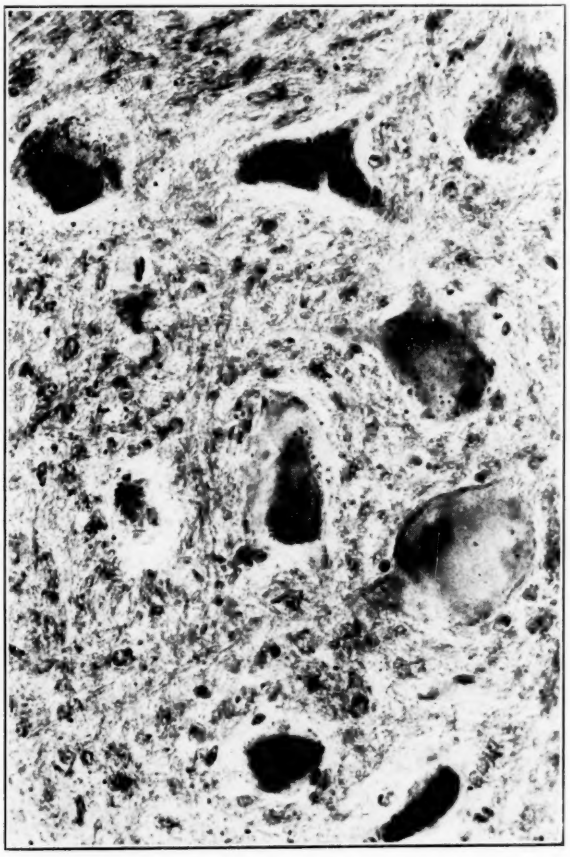

Fig. 2.—Herxheimer's method for fat (×325). Anterior horn cells in lumbar region. Orange-staining globules of lipoid material in all of the nerve cells (black in the illustration).

The Marchi stain showed fiber degeneration in the entire periphery of the cord and in the posterior columns. Spiller[95] found in a dog killed forty-two days after repeated stovain spinal anesthesias that the lumbar cord showed: (1) degeneration in the posterior columns and in the intramedullary portion of the anterior roots, and (2) swollen axis cylinders in the anterior and posterior roots. Davis and co-workers,[27] using four spinal anesthetic preparations with procaine as their chief constituent, found in dogs: (1) a slight inflammatory reaction in the

spinal leptomeninges; (2) retrograde degeneration of the anterior horn cells still present in slight degree ninety days after the injection; (3) swelling and fragmentation of axons in the lumbar and sacral regions up to twenty-one days after the injection; and (4) peripheral demyelinization in the lumbar cords twenty and thirty days after injection. Lundy and co-workers[68] in the same experiment obtained the same result in the axons and myelin, but found no meningeal or ganglion cell

Fig. 3.—Spielmeyer's method for myelin (×34). One lateral column and adjoining gray matter in lumbar region. Note zone of peripheral demyelination of varying thickness.

changes. Winograd and Rosenbloom,[107] using spinocaine in dogs, found only early irritative changes (cloudy swelling of ependymal cells) in the spinal cord, with no degenerative changes. Wossidlo[110] believed that there was "no pathologic-anatomic reason to warn against the use of spinal anesthesia."

We have been able to find in the literature 6 clinical cases of late death following spinal anesthesia in which there were symptoms of cord involvement and in which autopsy studies were made.[20, 58, 66, 75, 79] In

3 of these cases[20, 66, 79] there was either a demyelinization of roots and periphery of the cord in the lower spinal canal or retrograde degeneration of ganglion cells or both.

In our case, since the changes in the spinal cord closely parallel those found following spinal anesthesia in animal experiments, and in 3 of the previously reported clinical cases, it is our conclusion that they are primarily caused by the spinal anesthetic, although in this case it also seems likely that the patient's extremely poor general condition made her spinal cord much less resistant to the toxic action of the anesthetic.

SUMMARY

From this report it is obvious that a wide variety of neurological complications, either immediate or remote, may follow spinal anesthesia. The tables summarize the pertinent data. Undoubtedly many complications will go unrecognized unless careful postoperative neurological studies are made. That some of these complications may appear days, weeks, or even months after spinal anesthesia should be of definite interest to internist, surgeon, and anesthetist. Fortunately, these complications are relatively infrequent and should not deter the use of this anesthetic when it is indicated.

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Review of Recent Meetings

REPORT OF THE MEETING OF THE NORTH CENTRAL BRANCH OF THE AMERICAN UROLOGICAL ASSOCIATION, INDIANAPOLIS, IND., SEPT. 25-27, 1939*

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THE North Central Branch of the American Urological Association met at Indianapolis, Ind., on Sept. 25 to 27.

C. C. Higgins, Cleveland, Ohio, discussed present opportunities for training in urology, emphasizing that only the rudiments can be taught to undergraduates because of the demands made upon their time by the other specialties. While relatively few clinics offer really adequate training in urology at present, the number of those that do is increasing. The efforts of the American Board of Urology to catalogue residencies and fellowships and to elevate the standards of training and practice should be of increasing assistance to those seeking training in the future.

J. B. Morgan, Cleveland, Ohio, discussed the indications for pneumopyelography, thus far little used. It is of value chiefly in demonstrating radiotransparent calculi when other methods fail, and in such circumstances it may be invaluable. While there is theoretically some danger of air embolism, Morgan has had no mishaps in a considerable series of cases.

L. P. Dolan, Toledo, Ohio, presented a case of sudden collapse with allergic manifestations and death following the intravenous injection of diodrast. He feels that diodrast and similar agents are contraindicated in any patient with a history of allergy, although there is little mention of such a contraindication in the scientific, and none in the commercial, literature on excretory urography.

N. J. Heckel, Chicago, Ill., employed testosterone propionate in benign hypertrophy of the prostate, undescended testis, and sterility, quite without success. Sperm counts made before, during, and after treatment indicate that testosterone impairs spermatogenesis. In Froelich's syndrome and hypogonadism, testosterone caused a definite growth of the penis and of the pubic hair, and was useful.

J. S. Eisenstadt, Chicago, Ill., operated upon thirteen patients who had received anterior pituitary-like substance for undescended testes. In those who had received a total of more than 6,000 rat units, the testis was smaller and softer than usual, suggesting injury by the hormone, although the evidence of a definite connection between the use of hormone and the size of the testis seems far from clear if one considers how often the undescended organ is not quite normal.

*Only those papers actually heard by the author are reviewed herein.

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In the ensuing discussion of hormones, **W. E. Lower**, Cleveland, Ohio, spoke very hopefully of the possibilities of endocrine therapy in prostatism, although success is not as yet at hand.

Russell Herrold, Chicago, Ill., reported that sulfapyridine had cured 75 per cent of the cases of gonorrhea treated by him in from five to seven days; 15 per cent were cured by a second course, and 10 per cent proved refractory. If this is borne out by subsequent experience, gonorrhea may be regarded as very nearly conquered.

On the second day, **Harry Goldblatt**, Cleveland, Ohio, reviewed his experimental work upon hypertension. In addition to the experimental proof that renal ischemia, even when unilateral, may cause hypertension, clinical evidence is now accumulating. The mechanism by which ischemia produces hypertension is not yet fully known. Goldblatt states that it is only one of a number of factors which may produce high blood pressure, and that its relative importance is not yet known. The reviewer feels that many an innocent kidney will be removed from patients with hypertension before this fact becomes as apparent to urologists and surgeons as it is to Dr. Goldblatt.

W. N. Taylor, Columbus, Ohio, described his experiences with suprapubic prostatectomy and transurethral resection; he was unable to believe that the latter operation was preferable in 90 per cent or more of the cases, as is held by some. In his own hands the mortality of the two operations was not very different. Open operation is easier and more certain in the large prostate, although he remarked that the term "large" meant various things to different urologists.

The paper of **C. R. Marquardt**, Milwaukee, Wis., on 74 cases of injury to the urinary tract by violence may be summarized as follows: In diagnosis excretory urography and cystography are invaluable. In treatment, conservatism and alert observation are the keys to success with renal injury. Surgical drainage to the injured bladder is imperative. The traumatized urethra may respond to catheter drainage, while the ruptured organ must be repaired surgically. In any case, a stricture must be anticipated and dilatations begun very early if stricture is to be avoided.

Ureteral injuries during gynecologic operations were considered by **I. J. Shapiro**, Chicago, Ill., and **George Ewell**, Madison, Wis. If injury is discovered at the time of operation, repair over a catheter is the method of choice, and extraperitoneal drainage is essential. If the lesion is discovered during early convalescence, nephrostomy on the obstructed side is far safer than reopening the abdominal wound. Later, an occluding ligature may be absorbed and continuity restored spontaneously, or the severed ureter may be united end-to-end over a catheter and reimplanted into the bladder or even into the bowel. Successful examples of various methods were supplied, including some in which repair or reimplantation was technically impossible, and in which nephrectomy was the best solution.

On the last day, **J. L. Emmett**, Rochester, Minn., reported a series of cases in which urinary retention, accompanied by little or no visible evidence of prostatic enlargement, even in the presence of lesions of the spinal cord, such as tabes dorsalis, had been relieved by transurethral resection. This possibility is well known to most urologists, but needs dissemination among other medical men, who, with the best of intentions, deny relief to patients with "cord bladder" or retention of the urine without palpable prostatic enlargement. It is to be remembered that such retentions may occur in young men.

Charles D. Ehlert, Alton, Ill., reported a case in which appendicitis produced dysuria, pyuria, and urinary frequency with fever and which was mistaken for pyelonephritis until peritonitis developed and led to a fatal outcome. The more usual error consists in removing a normal appendix for symptoms actually due to ureteral calculus or seminal vesiculitis. While the average case is usually readily diagnosed, the exceptional one may demand great diagnostic acumen.

Ruben Flocks, Iowa City, Ia., discussed some interesting studies of the calcium metabolism in patients with renal lithiasis; in two-thirds of the cases he found an increase in calcium excretion on the affected side whether the calcium content of the diet was low or high. When urine was collected separately from the two kidneys, excretion was usually higher on the affected side. He pointed out that acidification of the urine in cases of increased excretion, while usually desirable postoperatively to prevent recurrence of stones, at times might cause further increase in excretion of calcium and so favor stone formation. In patients whose excretion is normal this does not hold.

Parke G. Smith, Cincinnati, Ohio, described the successful use of ureteroureteral anastomosis. The lower ureter had been demaged at a high enough level so that it could not be reimplanted into the bladder; it was divided above the site of injury, carried across beneath the peritoneum to the other ureter, and anastamosed to it; subsequent urograms showed both kidneys to be normal. **C. C. Higgins,** Cleveland, Ohio, reviewed a similar case of his own. While this is an admirable achievement, one cannot help but wonder whether, under most circumstances, it would not be wiser to implant the affected ureter into the bowel or to remove its kidney, rather than to jeopardize the opposite kidney by meddling with its ureter.

F. E. B. Foley, St. Paul, Minn., presented an interesting example of embolism of the renal artery with the following features; an elderly woman with a cardiac lesion developed sudden severe renal pain. Cystoscopy demonstrated anuria on the affected side but with a normal retrograde pyelogram. Subsequent excretory and retrograde pyelograms at intervals showed a functionless kidney which was still shrinking a year later, thus confirming the diagnosis.

THE SWEDISH SURGICAL SOCIETY

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THE spring meeting of the Swedish Surgical Society was held in the surgical amphitheater of the Academic Hospital, Uppsala, Sweden, on Saturday, May 20, 1939. Before proceeding to a discussion of the meeting, a very brief review of the organization of Swedish surgery will be given for the benefit of American readers.

As in most other countries, the medical schools of Sweden are a strong determining factor in the advance of surgical teaching and practice. There are three separate medical schools in three towns: Lund in the south, Stockholm in the central part, and Uppsala, an hour's train ride north of Stockholm. This ratio of three schools to 6,000,000 inhabitants is much the same (1:2,000,000) as in the United States with 67 schools to 127,000,000 (1:1,800,000). **Petrén** is the

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professor of surgery at Lund and **Nyström** at Uppsala, while Stockholm has two surgical clinics of university rank, with **Söderlund** and **Hellström** as their heads. The former is at the Serafimer Hospital and the latter at the Maria Hospital. It is of interest that all of these men except Hellström are at or near the retiring age. Petrén just retired this summer, while in May, 1939, Hellström took over the post left open by the retirement of Einar Key. This year and those immediately following thus will see a sweeping change in the leadership of the Swedish university surgical clinics. This is especially true because of the sudden death of the famous Hybbinette, honorary professor in Stockholm, this spring.

This brings up the question of the meaning of the term "honorary professor of surgery" in Sweden. When Hybbinette was alive, there were four such professors: Hybbinette and Giertz in Stockholm and Johannson in Gothenburg (Göteborg) in general surgury and Olivecrona in Stockholm in neurosurgery. These men are appointed honorary professor in recognition of accomplishment, even though they are not university professors or "ordinarius." When it is remembered that some of our American schools may have as many as a half-dozen full professors in one department, the distinction of becoming so in a land where there are only four such positions possible in the whole country is more manifest and the need for a few honorary professorships is also obvious. The honorary professorships at present are held by three men who well deserve them. **Professor Giertz** (pronounced *Yetsch*) is at the Sabbatsberg Hospital in Stockholm and his department is definitely of university caliber, being more scientific than many university clinics in some countries. Similarly the clinic at Gothenburg, which already has scholastic connections because of the presence of a medical academy or nonuniversity medical school, is of a high order. Its leader, **Professor Johannson,** the originator of the threaded flanged nail for collum femoris fractures, is an excellent surgeon and scientist. The neurosurgical clinic of **Professor Olivecrona** needs no comment.

Besides these professorial clinics, there are numerous surgical departments in community hospitals scattered throughout the country. One of the best known of these is that of **Bohmansson** in Örebro, which is a model of organization. Socialized medicine as existing in Sweden today has advantages and disadvantages, a discussion of which is too complex to be made at this time. However, mention will be made, without comment, of the recent doctor's strike at the Serafimer Hospital, Stockholm, where surgeons of university ranking with positions corresponding to associate professors in this country protested because their full-time salaries of $1,250 per annum were to be cut.

The present meeting of the Swedish Surgical Society consisted entirely of papers given by members of the Surgical Clinic in Uppsala and represented a cross-section of the work of that department under the leadership of **Professor Gunnar Nyström.** Visits to many European surgical clinics indicated that this was one of the most progressive and best organized in Europe. **Nyström** is one of the great Swedish surgeons of all time and the character of the younger men in his clinic indicates a continuance of the high standards he has set. The following papers were given:

Henry N. Harkins, Detroit, Mich. (By invitation.): **Physical Factors in Surgical and Traumatic Shock.**—The essential features of this paper have already been reported in the American literature and will not be repeated here.

Harald Lundberg, Uppsala: **Phylactotransfusion.**—Dr. Lundberg demonstrated three cases of septic infection treated with phylactotransfusion. These were all of the phlegmonous type without tendency to limitation, but after

the transfusions (in two cases only one, in the third, three transfusions) the processes were definitely limited and soon healed. The author demonstrated at the same time some results of experimental investigations on rabbits on this subject. These animals were inoculated intracutaneously with staphylococcus and streptococcus organisms and then given a phylactotransfusion (the donor being sensitized only once, three hours before the transfusion). The inflammatory areas on the test animals were then excised at intervals and examined microscopically. It was found that these areas were more completely and rapidly limited on the test animals than on the controls, a difference in reaction which is fully seen from eighteen to thirty hours after the transfusion. These results are in full accord with clinical experience. As this difference in reaction seems to be fully developed during only a short period, the author suggested that the phylactotransfusion be repeated, if necessary, after twenty-four to forty-eight hours.

Gunnar Redell, Uppsala: **Are Anastomotic Operations a Legitimate Procedure in Choledocholithiasis?** In this paper Redell made a comprehensive survey of the literature on the subject as well as a review of the cases treated at Uppsala. This report is to be published in full in the near future and so is abbreviated here. It promises to be the most complete survey ever made of the subject.

Karl Erik Grott, Uppsala: **Sarcomatous Embolism in Left Femoral Artery With Extensive Postembolic Thrombosis. Treatment With Embolectomy and Injection of Heparin Solution in the Artery.**—A married woman, aged 36 years, had an amputation of the right leg in 1937 for sarcoma tibiae. In February, 1939, roentgen examination showed pulmonary metastases. Embolism of the left femoral artery, possibly from a tumor embolus from a pulmonary vein, occurred on February 27, 1939.

Operation was performed ten hours after the onset of symptoms and an embolus and postembolic clot, 8 cm. in length, were removed through an arteriotomy. Extra-arterial massage gave only temporary improvement of the circulation. Through another incision another postembolic clot of not less than 75 cm. came out, but the circulation still showed only a slight improvement. Two more attempts to restore it failed, intra-arterial eupaverin helping temporarily. New clots always appeared after suturing the arteriotomies and the prognosis for the life of the limb seemed very poor. Indeed, the passage in the artery was cleared for the fifth time by arteriotomy and immediately after the incision was sutured 100 mg. heparin (2 c.c. of a 5 per cent solution) was injected in the artery just above the incisions. The circulation in the leg was now definitely restored. Some more heparin and eupaverin were given the following days. Viability of the limb was good and there were no postoperative complications. The patient died a month later from her pulmonary growths.

At necropsy the left common femoral artery showed perfect passage with only a few very small clots attached to the wall. Microscopic examination of the embolus showed sarcomatous involvement of the same type as the primary tumor and the lung metastases.

The impression was gained that in such a case with a very pronounced tendency to form clots at the operative site, the adjuvant treatment with heparin made it possible to get a definite restoration of the circulation after removal of the embolus and the postembolic clots. The intra-arterial injection of heparin at the desired site of action would seem to be more logical than intravenous administration.

Gunnar Nyström, Uppsala: **Multiple Nails for Fracture of the Collum Femoris.**—Professor Nyström's method is to use three small flanged nails of his own construction which are inserted in different directions after a careful x-ray-controlled reposition. The advantages of this method are twofold, the fixation of the head is better than when only one large nail is used and the head is less maltreated, the vessels being preserved and late necrosis prevented. The patients stay in bed for three months, although movement is allowed during most of this time, and then they are permitted to walk.

Gunnar Nyström, Uppsala: **Case of Pulmonary Lobectomy for Cancer.**—A woman who had previously been operated upon for carcinoma of the uterus developed a metastatic lesion in the left lung. Because of slowness of the growth and lack of other evident metastases, operation was decided upon. After a previous artificial pneumothorax in several stages, the thorax was opened by extirpation of most of the left seventh rib. The hilus was cut through after ligation; the lumen of the upper main bronchus was coagulated by diathermy, sutured, and covered by a flap of the lower lobe; and a left upper lobectomy was performed. The anesthetic used was evipan. A serothorax developed which organized and at the end of three months the patient felt quite well.

Dr. Lundberg, Uppsala: **A Case of Luxatio Humeri Posterioris Retroglenoidalis.**—The caput humeri could not be kept in position by means of any fixation, but reluxated immediately. For that reason the patient, a man 45 years of age, was operated upon by the method of Hybbinette-Eden. The shoulder joint was opened from behind, the acromioclavicular joint opened, and the acromion chiseled through and drawn laterally. A tibial graft 2 by 5 by 0.3 cm. was put under the periosteum of the back side of the neck of the scapula, extending over the posterior margin of the glenoid cavity about 1 cm. By this means the collum humeri was prevented from sliding back. After fixation of the arm for four weeks, exercise was started and movements became normal after three months.

Gunnar Nyström, Uppsala: **Case Demonstration of Scalenus Syndrome.**—From the last cervical transverse process, which was about 4 cm. long, a fibrous membrane extended down to the first rib. The process and the membrane were removed, with improvement.

Dr. Lundberg, Uppsala: **Narcotal, a New Intravenous Anesthetic.**—Lundberg related the experiences at the Uppsala Clinic with a new Swedish preparation for intravenous anesthesia. In a large series of cases they had good results with no complications. This anesthetic has the following composition:

Isopropyl-β-bromallyl-N-methl-malonylcarbamidnatrium	— 0.11 Gm.
Phenyldimethylpyrazolon	— 0.10 "
Glycerin	— 0.10 "
Aqua Redest	ad 1 ml.

Book Reviews

Cancer of the Colon and Rectum: Its Diagnosis and Treatment. By Fred W. Rankin, M.D., and A. Stephens Graham, M.D. Cloth. Pp. 358, with 133 illustrations. Springfield, Ill., 1939, Charles C. Thomas, Publisher. $5.50.

The experience and study alone which have been compounded to create this book make of it a splendid monograph. In addition, the subject matter is treated in a well-ordered manner and the book is well written.

The senior author has been known as one of the leading exponents of surgery of the large bowel. This judicious monograph justifies fully the credence and authority which his expressions have been lent.

The authors favor the exteriorization operation for excision of the left colon for malignancy when feasible. They trace the development of this operation and the abdominoperineal operation for cancer of the rectum, to which procedure they are partial. For malignancy in the right half of the colon, the authors advocate a one-stage aseptic excision, in which procedure the senior author has had a long experience.

In acute obstruction of the colon the authors favor the performance of cecostomy as the decompressive operative procedure of choice. From his own experience this reviewer cannot agree that an aseptic decompression can be made on the cecum in the presence of great distention as satisfactorily as on the transverse colon. Spontaneous tension perforation of the cecum has apparently not been a frequent occurrence in the experience of the authors. The authors point out quite rightfully that a permanent opening in the transverse colon is not as satisfactory as one in the left inguinal region. The value of an antecedent diversion of the fecal stream by colostomy when the continuity of the gut is to be re-established following a one-stage excision of the left colon is supported by impressive figures.

This text constitutes a worth-while addition to the literature of the management of malignancy of the large bowel and can be recommended enthusiastically.

The Essentials of Modern Surgery. By R. M. Handfield-Jones, University of Cambridge, and A. E. Porritt, Editors. Cloth. Pp. 1,142, with 501 illustrations. Baltimore, 1938, Williams & Wilkins Company. $9.

The editors' expressed object in presenting this text under multiple authorship was to prepare a textbook intermediate between the two or more volume work and the short one volume text aimed at "the less enthusiastic student with sufficient easily assimilable material with which to satisfy the examiners." This unpretentious objective the authors have beyond question achieved.

The concentration of effort of fifteen authors upon this task lends authority to the text; especially is this true when an author writes upon a subject wherein his interest has become well known through original and worth-while contributions to the field.

One criticism of most current surgical texts which can with all fairness be leveled against this one, too, is the lack of specific information concerning the

risks, as well as the results, of operation. The student has a right to expect information of this sort in a text. Another serious defect is the omission of textual references to original sources. It would almost seem that a studied effort had been made to eliminate completely this stimulating influence upon students of mentioning the names of those whose contributions extend knowledge within the field under consideration.

It may be questioned whether a textbook on general surgery may include justifiably chapters on diseases of the skin, the ear, and affections of the nose and accessory sinuses, when indications for, and the risks and results of, operations are treated in a superficial manner.

Rontgendiagnostik des Chirurgen. By Prof. Dr. Otto Kingreen. Paper. Pp. 325, with 527 illustrations. Leipzig, 1939, Johann Ambrosius Barth. RM 32 bound, and RM 30 unbound.

This volume follows the usual form of German language texts. It is concerned chiefly with the application of the roentgen method in the diagnosis of surgical conditions, but there is a rather general discussion of the whole field of x-ray diagnosis. An introductory chapter concerning methods of x-ray examination, equipment, and technique of x-ray diagnosis is very informative. The detailed discussions of foreign body localization and of fractures will be of considerable value to surgeons. There is, however, surprisingly little attention devoted to the roentgen findings in the acute abdominal lesions, such as intestinal obstruction, or to a description of the appearance of the thorax and the gastrointestinal tract following surgical procedures. The illustrations of roentgenograms are numerous, well chosen, and well reproduced, but there are surprisingly few diagrams. A bibliography is not included. While a book of this kind will be useful to surgeons and radiologists, it adds little to the textbooks of roentgen diagnosis already available.

Roentgen Technique. By Clyde McNeill, M.D. Cloth. Pp. 315, with 274 illustrations. Springfield, Ill., 1939, Charles C. Thomas, Publisher. $5.

The importance of roentgenograms of a high technical quality cannot be overemphasized, hence any contribution to this subject is important. Although it does not pretend to be a complete study of roentgenologic technique, this volume contains valuable material in this field. Essentially it is devoted to a pictorial demonstration of positioning for various roentgen examinations. Theoretical considerations, the physics of roentgen technique, details as to equipment and darkroom procedure are largely omitted. With very few exceptions, all the usual x-ray technical procedures are described with the various positions which are desirable for each type of examination. Each anatomical position is beautifully delineated both by diagrams and actual photographs. The technique of certain newer procedures, such as kymography, tomography, pelvic measurements, and others, are thoroughly elucidated. While there are some references to roentgen diagnostic findings, these are purely incidental. The details of roentgen anatomy which are given are substantially correct, although many important details are omitted or presented in gross form. The data on ossification centers, for example, while accurate enough for orientation purposes, are not to be relied on

for actual diagnosis. The format, printing, and quality of the illustrations are excellent. The book will be useful both for roentgen technicians and for physicians who find it necessary to do roentgenography, but it must be supplemented by other texts.

Roentgen Diagnosis of the Extremities and Spine. By Albert B. Ferguson, M.D. Pp. 465, with 512 illustrations, including 508 x-ray plates, New York, N. Y., 1938, Paul B. Hoeber, Inc. $12.

In this text the author presents the wide experience of the New York Orthopedic Hospital with roentgen diagnosis of lesions of the bones and joints. Even a casual perusal of the text will indicate that the author is well oriented in the pathology of the disorders which he describes; that he is familiar with the clinical manifestations and course of the diseases which he undertakes to discuss, as well as the roentgen signs of the disease, which is his major interest. There are many subtended footnotes throughout the text in which many cross references to cases described and illustrated in the text are made. This should prove a very useful and practical text not alone to roentgenologists, but also to orthopedists and general surgeons. The illustrations are uniformly good. The discussions and descriptions reflect a large, broad experience into which the author has injected a goodly portion of critical study of his own material as well as that of others. Bibliographic references to original sources would have enhanced the value of the book.

The Art of Anesthesia. By Paluel J. Flagg, M.D. Ed. 6, revised. Cloth. Pp. 491, with 161 illustrations. Philadelphia, 1939, J. B. Lippincott Company.

To revise adequately a book on any phase of medical science is a stupendous undertaking. The rapid progress made in anesthesiology during the past twenty years makes the satisfactory bringing up to date of a book written two decades ago exceptionally difficult. The original title, *The Art of Anesthesia,* has been retained for this sixth edition of Dr. Flagg's book. In spite of the title, some science has crept in, whether with or without the author's intention it is difficult to determine.

In the preface to the sixth edition the author raises the question of terminology, suggesting the word "pneumatology" in place of the current "anesthesiology." It will be remembered that John Snow, the first great anesthetist, in 1847 objected to "anesthesia" and voted for "narcosis." However, common usage is probably the determining factor in such matters, and "anesthetic," "anesthesia," and "anesthesiology" doubtless will survive. In this reviewer's opinion, the author is correct in his contention that the anesthetist's necessary daily experience with the depression accompanying pain relief makes him the logical member of the hospital staff to be concerned with the therapy of acute respiratory and possibly circulatory disorders.

The following is a quotation from the preface: "The Pneumatic Institute of Sir Thomas Beddoes provided a nucleus about which the pneumatologists of the period brought to a focus the earlier work of Hickman, Priestly, and others." Beddoes' Pneumatic Institute was discontinued as such in 1800 and Henry Hill Hickman was born in that year. Joseph Priestley spelled his name Priestley. The quotation is illustrative of many inaccuracies throughout the book, some of which are not so innocuous as these.

Evidence of careless editorial effort or of unfamiliarity with the abundant literature of the last few years is shown in many chapters on widely divergent subjects. For example, in Chapter III entitled "The Signs of Anesthesia," a heterogeneous handling of the physical changes accompanying increasing dosage of inhalation agents could have been as well written twenty years ago. It ignores some of the contributions made to the subject by Arthur Guedel, by the author's old preceptor, Albert Miller, and by others. The subjects of artificial respiration and fluid therapy are curiously touched upon in this same chapter and in a manner to confuse the reader and make difficult a comprehension of the author's ideas regarding physical signs. Again, in describing the use of nonvolatile agents for basal narcosis and for block anesthesia, the reviewer wonders whether lack of clear-cut statements regarding drugs, pharmacologic action, technique of administration, indications and contraindications is due to inexperience, lack of familiarity with current literature, or simply due to incomplete revision of the older text. Certainly the contents of these and other chapters cannot be taken as a safe guide to clinical practice.

As a record of the beliefs and practice of one individual anesthetist, this book is interesting reading and contains valuable information. As a text, it can scarcely be considered authoritative or representative of the current teaching and practice of anesthesiology in 1939.

Brazilian Medical Contributions. By L. Ribeiro. Paper. Pp. 181, with 62 illustrations. Rio de Janeiro, 1939, Livraria Jose Olympio.

The preparation of this volume recounting the most important aspects of the development of medicine in Brazil was occasioned by the Brazilian exhibit at the New York World's Fair. The avowed purpose of the book is to make available to the libraries and universities of the United States a small volume that will tell of some of the contributions that Brazil has made to medical science. At the same time it sketches the attempts that are being made to meet the health problems of that country. The book contains an assortment of unrelated chapters describing the various scientific institutes; the official public health structure of the country; the campaign against tuberculosis, leprosy, and yellow fever; the mineral spas of Brazil; the work of outstanding figures in Brazilian medical development; and summaries of three or four interesting programs of study. The book is of value to the reader who is interested in learning of some of the medical and health problems of a nation of which the average citizen of the United States has but the vaguest ideas. It is unfortunate that a book of this character should not have been submitted to the editorial and typographical scrutiny of one more conversant with idiomatic English, thus avoiding the peculiarities and stiltedness of style as well as errors that make the book hard to read. It is generously illustrated with pictures and diagrams.